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Reports on Public Health and Medical Subjects

No. 124

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their Use and Misuse

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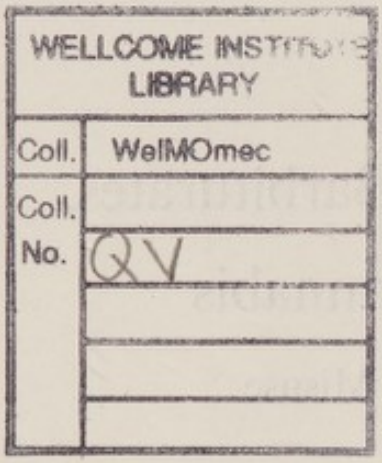

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PREFACE

The four reports which make up this volume were prepared by Sir Aubrey Lewis to assist the Standing Advisory Committee on Drug Dependence.

The section on cannabis is a summary of facts from the international clinical literature on that drug and has previously been published as Appendix 1 in the Report on Cannabis prepared for the Home Secretary and Health Ministers and published in 1968. However, it fits well with the reviews of the amphetamines, the barbiturates and LSD for which the Committee is also indebted to Sir Aubrey.

The abuse of psychotropic drugs is an important and urgent problem in Britain of interest to the professions and others concerned. The Committee therefore welcomed the opportunity of making the whole group of reports available in this series.

G. E. GODBER

December 1969

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AMPHETAMINES

Pharmacological Background

Effects of a moderate dose

The effects of a moderate dose of amphetamine or of one of its congeners are euphoria, wakefulness, increased initiative, and heightened sense of confidence and ability. These effects depend on the mental state and personality of the recipient as well as on the dose.

Acute intoxication

Some people develop headache, anxiety and confusion on a small dose, but as a rule acute intoxication has been the result of a single dose that was many times larger than the therapeutic dose. The physical toxic effects, due to the drug's sympathomimetic action and stimulation of the central nervous system, are less conspicuous than the mental changes, which consist chiefly of auditory and visual hallucinations and of paranoid delusions. In predisposed persons the somatic effect may, however, be alarming and even fatal. Clinical observations suggest that the combination of a mono-amine oxidase inhibitor with amphetamine increases the risk of poisoning. Children who take an excessive quantity of amphetamine become restless and cannot sleep; they are very talkative and may be hallucinated. The acute condition may take twenty-four to forty-eight hours to clear up during which physical changes may occur, such as vomiting, dilated pupils, tachycardia and, in rare cases, convulsions and collapse.

Laboratory studies

Because of their fatigue-lessening properties the amphetamines were investigated during the war in psychological and pharmacological laboratories. Since then, and in particular because of their effect on athletic performance, they have been further studied under experimental conditions.

It has been shown that if an appropriate dose is given at an appropriate time amphetamine prolongs the time during which a man can perform hard physical work and that it can improve athletic performance in swimming, running, and putting the weight. The drug lowers reaction time and improves coordination and steadiness. It is effective in restoring performance that has deteriorated and in maintaining a high level of proficiency in responding to pointer signals (monitoring). It can temporarily hasten conditioning and learning some motor skills. It does not, however, improve intellectual performance except when this has been lowered by fatigue or lack of interest. It disturbs judgment of time intervals.

These findings, predominantly favourable to the use of the drug, are contradicted or modified by some others. It has been found, for example, that amphetamine does not produce an improvement in performance if the subject is alert, fresh and interested. Many of the discrepancies can be accounted for by differences in dosage or in the tests employed, e.g. for determining reaction time. Relatively little study has been made of the basic psychological changes brought about by amphetamine; the need for this is illustrated by a strictly controlled

study carried out by Beecher and his colleagues who found that students of Massachusetts Institute of Technology did better on a digit-letter coding test after they had taken amphetamine than before, but that they showed no improvement in their ability to solve calculus problems, though both tests might be regarded as measures of cognitive capacity. Most laboratory studies suggest that moderate doses of amphetamine, e.g. 10 to 15 mg, in normal adult subjects, produce only slight enhancement of performance with no increase in errors in some sensori-motor and perceptual tests, but that conspicuous enhancement may be observed when the amphetamine has been given to someone whose performance is reduced by fatigue or lack of sleep. There is, however, much variation from person to person, some showing maximal response to a relatively small dose, others becoming depressed or sleepy instead of excited, active and confident.

Effects on athletes and students

The uncertainty that prevails regarding the desirable and undesirable effects of amphetamine is exemplified by the conflicting assertions about its effect on athletic performance. Thus it is said to increase static muscular strength but to have no effect on muscular endurance, e.g. as determined by "chinning the bar".

Three Austrian investigators conclude that athletes can derive very little benefit from the use of amphetamine in sports which depend on fast responses or sequences of responses. In a rigorous experiment, fifteen expert swimmers and fifteen non-experts were given amphetamine, 14 mg/70 kg of body weight, and it was found to improve their performance to a similar extent in the two groups. Some of the swimmers were, however, impaired in their performance by the drug, which had been given two to three hours before the test. Significant improvement occurred in 75 per cent of the subjects. More were helped by amphetamine when they were tested after a rest than when they were tested under fatigue conditions.

A group of volunteers drawn from the population of a prison was given a single dose of dexamphetamine or methylamphetamine and a series of tests carried out to determine the changes produced in intellectual functioning; it was concluded that definite beneficial effects in both objective and subjective indices of intellectual performance were forthcoming.

The obvious difficulty in generalizing from such findings, in which individual variation plays a part, is evident in a study made on medical students, 44 per cent of whom had used amphetamine. Fifty-five per cent of them had observed some deleterious effect such as edginess and nervousness, irritability and difficulty in logical thinking; depression and fatigue after the main drug effect had worn off, and three of the students believed that they had failed an examination because they had taken the drug beforehand, but an approximately equal number of students said there were no deleterious effects they could record. Alongside the reported unpleasant effects of amphetamine were assurances by students that they had noticed a beneficial effect from the amphetamine in the form of either reduced fatigue, reduced appetite, increased alertness, increased span of attention or increased motivation. It is clearly necessary to distinguish between purely subjective changes which are reported and objective changes in performance and behaviour generally.

Effects on the mentally ill

Intoxication has been produced by intravenous injections of methylamphetamine given to mentally ill patients in order to overcome inhibitions and promote abreaction. Some of the toxic phenomena thus elicited were in hypomanic patients who then exploded into manic excitement; in some depressed patients it brought about an augmented degree of misery; in patients with catatonia it aggravated the catatonic features and in schizophrenic patients who were not catatonic it evoked catatonia.

It seems that dexamphetamine by mouth had little or no effect on the sleep pattern and the appetite of chronic schizophrenic patients who were given the drug because they were obese.

Teratogenic and other somatic effects

A possible teratogenic effect of phenmetrazine administered during the first six weeks of pregnancy has been canvassed on the strength of two doubtful cases. In a similarly tentative and inconclusive way, acute myeloblastic leukaemia has been related causally to amphetamine in a man who developed the blood condition after having taken massive doses of amphetamine for more than two years. A fatal outcome attributed to methylamphetamine has been described; the patient was a man of twenty-two in whom acute renal failure came on with hyperpyrexia and jaundice after he had swallowed 140 mg of the drug. However, the statement by Bonhoff and Lewrenz in their comprehensive monograph of 1954, that death from amphetamine is very rare, still holds good. They listed only three such fatalities, all questionable, but since then more have been reported.

Therapeutic Uses

Depression: A common—probably the commonest—therapeutic use of amphetamine has been for the relief of mild depression, in which difficulty of concentration, tiredness and slowing of mental activity are the chief complaints. Reports of impressive benefit have been published, but whenever a controlled trial has been carried out the results have failed to support such claims. Comparison of dexamphetamine, and of dexamphetamine plus amylobarbitone sodium, with imipramine and with a placebo (lactose) in a double blind trial failed to show any advantages over the placebo of the amphetamine preparations, either with or without barbiturate, i.e. the dexamphetamine was no more beneficial than lactose. Indeed, in another English study, carried out by general practitioners on over one hundred depressed patients, the placebo-treated group showed more improvement than the dexamphetamine-treated group.

Schizophrenia: Schizophrenia has also been treated with amphetamine, but in a large-scale American study of 520 chronic schizophrenic subjects receiving maintenance doses of chlorpromazine there was no advantage in the amphetamine over placebo; disadvantages were that the patients became more hostile and showed "intellectual disorganisation" when under the influence of amphetamine. However, in another American trial, it did appear that methylphenidate was useful to counteract the sedative effect of phenothiazine in schizophrenic patients.

Obesity: Amphetamines have an undoubted effect in reducing appetite. They have, therefore, been much used in helping fat people to reduce their food intake. Some writers, like Leake in his 1958 monograph, see few disadvantages in this: "There has come a great opportunity for physicians to practise effective preventive medicine through the control of overweight. The amphetamines now seem to be the best available drugs to aid in reducing weight." Others have found that the effect does not last, even if the dose is increased, and that interference with sleep and the feeling of fatigue which comes on when the action of the drug has worn off are accompaniments which often lead to increased intake and dependence. Psychoses and other signs of intoxication may develop, though here again therapeutic enthusiasts like Leake maintain that "the low toxicity of the amphetamines and their relative freedom from any harmful effects, make it possible to prescribe them safely for the majority of obese patients, in conjunction with rigid dietary control". A large number of published case reports dispel this comforting picture. At best the amphetamines can only offer a prop. The more a patient's obesity is accompanied by anxiety and neurotic symptoms, the less possibility of success is there from amphetamine administration. The consensus of opinion about the "anorexigenic" use of amphetamines is succinctly put by M. J. Albrink: "Appetite depressant drugs of the amphetamine group are effective for only a few weeks. Dependence on their stimulating effects occasionally makes withdrawal a problem. Such drugs have no demonstrated role in the long term management of obesity."

Hyperkinesis and behaviour disorders in children: Amphetamine has been much used for the treatment of hyperkinetic children and of children with behaviour disorders. Although earlier accounts of its good effect have been shown by later and more critical studies to be overdrawn, there is satisfactory evidence that amphetamine improves behaviour and slows down over-activity, especially in those hyperkinetic children who have a normal electroencephalogram. Comparison of the effects of amphetamine with those of chlordiazepoxide and of diazepam in "double blind" trials illustrates its superiority over these substances in hyperkinetic children. Another group of American investigators found that methylphenidate had little or no effect on rote learning but improved the maze performance of emotionally disturbed children. Investigators of the same group have recently shown that the behaviour of children with learning problems may be improved by amphetamine, probably because of improved drive and assertiveness, zest and interest. Good responses, however, may be ephemeral. A group of boys in a training school for delinquents was given dexamphetamine in a controlled experiment and showed appreciable improvement at the end of the treatment, but three weeks later this was no longer evident.

Narcolepsy and other disorders

Amphetamine is effective in controlling the sleep attacks of narcolepsy. This can be, in fact, the one sure and justifiable use of amphetamines in therapeutics. It can also be useful in counteracting undesirable effects of other drugs, e.g. the sleepiness due to drugs given for the control of epilepsy, or the dystonic effect of phenothiazine drugs. It has been tried for stuttering, petit mal and given intravenously for acute barbiturate poisoning.

Combination with other drugs

The combination of amphetamine with amylobarbitone is popular and the observations of clinical workers and of psychopharmacologists support its vogue, though the associated risk of barbiturate dependence and of psychosis cannot be neglected. Various combinations of amphetamine with chlorpromazine or other phenothiazine derivatives have been put forward but there is little to justify their use. As is common in the history of drug dependence, Satan has been used to drive out sin: thus, amphetamine has even been recommended as a treatment of morphinism and for alcoholism.

Tolerance, dependence and effects of withdrawal

Practically all observers are satisfied that tolerance develops to this group of drugs, though it is conceded that some people continue to take a small dose for many years without feeling any need for increasing it. Psychological dependence is also well attested. There may be an overpowering desire to take the drug and to enjoy its effects. There is, however, dispute about physical dependence, i.e. as to whether withdrawal symptoms occur which are due to somatic changes. The majority of those who have dealt with amphetamine addicts and observed the effects of withdrawing the drug abruptly hold that the symptoms seen on withdrawal are wholly psychological. But a few careful observers do not agree. They regard the tremendous hunger and the profound and prolonged sleep which ensue after a bout of amphetamine intoxication as a withdrawal syndrome. Others report that a delirious or confusional state comes on some days—up to twelve—after withdrawal. The case is reported of a twelve-year-old boy who had taken 20 mg of amphetamine daily for more than two years for "an impulse disorder" with hyperkinesis. He improved but, two weeks before he was admitted to hospital, the drug was abruptly withdrawn because he was sleeping badly. Ten days later he developed difficulty in concentrating, paranoid delusions, and impulsive behaviour; he also attempted self-mutilation. He was very active and could not sleep. He was disoriented and could not perform simple intellectual operations but there were no vegetative changes. After several days he gradually recovered and within two weeks was able to return to school.

Clearest evidence of a physiological withdrawal syndrome is provided by the electroencephalographic findings during sleep. Six addicts were studied to determine the proportion of nocturnal sleep spent in so-called "hind brain sleep" which has a characteristic encephalogram related to rapid eye movements and changes in muscle tension. Before the drug was withdrawn, and in spite of their having taken it for a considerable period, the EEG picture these patients presented was normal. Upon withdrawal, the "hind brain sleep" began very quickly after onset of sleep—within four minutes instead of the normal seventy minutes—and occupied up to half the night, whereas normally it would occupy about quarter of the night. The electroencephalographic pattern took three to eight weeks to return to normal unless the drug was restored, in which case it returned to normal immediately. Three of the six patients were also receiving barbiturate and this may have affected the electroencephalographic pattern. Interpretation of the finding would be easier if there were available some record of the "hind brain sleep" in a normal person to whom a single dose of amphatamine had been administered. However, the available data suggest that there

can be a slight physiological amphetamine withdrawal syndrome, other features of which, besides the changed electroencephalographic pattern, are irritability and depression. Nevertheless there is justification for the outburst by Dr. Kalant in her monograph; "These excerpts from the literature have been chosen to illustrate the degree of controversy that exists with respect to the addictive liabilities of the amphetamines. It is hoped that they also illustrate how the same evidence can lead to almost diametrically opposite judgments and conclusions when a scientific problem involves medical as well as ethical, social, cultural and other issues."

Misuse

Initial social influences

Two groups of persons can be recognised who misuse amphetamines. These are, in the first place, adolescents who are introduced to it by acquaintances and, secondly, older persons who are introduced to it by their doctor for reduction of food intake or for alleviation of mild psychoneurotic disorders. The two groups obviously differ in age, also in their attitude to the law, and in the duration of the habit. Many who begin with a prescription by their doctor for the drug with which they had not previously been acquainted, may ask for larger and larger doses; if the doctor proposes to discontinue the drug the patient demurs and (as is indicated by correspondence in the *British Medical Journal*) the doctor, unless he is strong-minded, gives in. Over-generous prescribing, no doubt based on clinical conviction about the efficacy and relative harmlessness of amphetamine drugs, is responsible for much habituation.

There is hardly any solid information about how adolescents get into the way of taking amphetamine. Scott and Willcox quote the frequent assurance they received that the tablets can be very easily obtained and that though there are "pushers" they are inconspicuous. "Most adolescent takers of amphetamine are initiated in clubs, dives and bars . . . a starting dose of five '*Drinamyl*' tablets is most usual, taken just before or on arrival at a dance or party, usually on a Friday or a Saturday night . . . the aim is to enjoy these social functions for all of one night or through a whole weekend. . . ." Excessive drinking of alcohol is rare and very few of the boys who take amphetamine take heroin or cocaine; "there is a healthy and widespread awareness of the dangers of these drugs". In these and other respects there is a striking similarity with what was reported by and about the Oakland marihuana users.

Social effects

Discussion on the relation of crime to the misuse of amphetamine has been somewhat vehement. Leake, in his monograph on "The Amphetamines, Their Actions and Uses", asserts that "the use of pep pills for thrills, whether by youngsters, adults or by oldsters, is not likely to lead to any serious difficulty, except in the case of unstable individuals who may break away from the social restraints of their group. This may happen without aid from the drugs. If it occurs when the individual has been using amphetamine the drug gets the blame rather than the society which sets the stage for misbehaviour, or the unstable emotional make-up of the individual." This is in striking contrast to what is

reported from Japan by Noda. This investigator states that 61 per cent of the 136 amphetamine addicts from Kurume had been involved in antisocial behaviour, and another Japanese writer states that half among 60 murderers convicted in Japan in May to June 1954 had some connexion with the use of amphetamine.

Apart from the Japanese statements, there are very few reported cases of crime directly attributable to amphetamine. Among these few, however, there are some (Binder, Keyserlingk, and especially Bonhoff and Lewrens) in which the recorded details point fairly strongly to a causal role of amphetamine in bringing about swindling and even murder.

In the study carried out at the London remand homes the offences of amphetamine-taking adolescents who were admitted were approximately of the same frequency, seriousness and type as those of the non-users of amphetamine who were admitted. The main deleterious effects of amphetamine were poor work record, deterioration of personal relationships, loss of interest in girlfriends, loss of self respect, and inability to concentrate on school work.

But on the other side of the picture are the reports from Sweden and, as already indicated, from Japan. In Sweden, the association between amphetamines and crime seems fairly strong. Among men released from gaol on parole, 32 per cent were amphetamine-takers, but it is by no means clear that the drug was either partly or mainly responsible for the crimes for which they had been sentenced. Of the prisoners examined by Professor Rylander in Stockholm, two-thirds of the amphetamine-takers said that the drug made them bolder and more confident. Professor Rylander considered that, in many respects, phenmetrazine intravenously was more dangerous than opium or morphine, which did not produce such rapidly devastating psychological and physical effects.

Allowing for the inherent difficulty in interpreting the possible causal nexus where crime and drug-taking are concomitant, it seems that the probability of a criminal outcome from amphetamine-taking is small.

Modifying and predisposing factors

There is evidence that the occurrence and severity of the addictive effects of amphetamine, as of other psychotropic drugs, depend on the psychological constitution and state of mind of the subject, his relationship to the person administering the drug, his social environment at the time, and his notion of the effects of the drug, as well as on its basic pharmacological action. There is, nevertheless, a sharp contradiction between observers as to the role of personality. Thus, whereas Durrant asserts that psychopathy, immaturity and personality defects, such as inadequacy and homosexuality, are consistently found to be the background of addiction, Scott and Willcox, examining a large series of boys and girls admitted to a remand centre, found that there were no major differences in personal factors between those adolescents who were taking amphetamine and those who were not. Scott divided the amphetamine-taking adolescents into a benign and a malignant group; whereas the former confined their indulgence to the weekends, took "*Drinamyl*" only, and did not increase the dose, members of the malignant group used different varieties of amphetamine recklessly, increased the dose or took it more frequently, and made poor personal relationships: "The same background and personal handicap is often observed in non-

amphetamine takers. Possibly some non-takers are so isolated that they are incapable of the necessary social competence to bring them to the clubs and bars where initiation occurs." There may be gradations between the sporadic user, the weekend user and the regular user.

Prevalence

It is impossible to obtain an exact or even an approximate measure of the extent to which amphetamine is being taken for other than therapeutic reasons in a given community or country. For example it seems that there is considerable variation among university students for, whereas an Argentine inquiry elicited that more than one-third of the first-year students took the drug on specific occasions, and that half the final year students took it to help them study longer, in an American medical school 44 per cent of the students said they had taken the drug, but of these one-fifth had done so on only one occasion. Of course data drawn from a sample of drug addicted persons tell a different story; in three detention institutions of the Department of Correction of New York City 93 per cent of the 10 per cent who were drug users were taking heroin, but 20 percent of the women and 3 per cent of the men also took amphetamine.

It is not even safe to calculate from prescriptions or medical case records the number of amphetamine-dependent persons who are receiving the drug from a doctor. Criteria of dependence are hard to apply. It was stated in the report of a Newcastle-upon-Tyne inquiry that the equivalent of 200,000 5-mg tablets were being prescribed per month, and that an unknown number of patients were also obtaining extra supplies. Rather more than 20 per cent of the patients who received amphetamine on prescription were judged by the doctors to be dependent on the drug; they had been taking it for long periods, they resisted its withdrawal, and they craved for it. In contrast to some other data, women preponderated among the amphetamine consumers. In this inquiry they amounted to 85 per cent of the patients receiving the drug on prescription. Dependence was found most often in the 36–45 age group. The commonest preparation prescribed was "*Drinamyl*" (35 per cent), the next commonest was dexamphetamine (21 per cent).

Japan and Sweden have had exceptionally disturbing experience with the misuse of amphetamines, especially with phenmetrazine and methylamphetamine.

At the end of the Second World War large stocks of amphetamine were made available in Japan, the military authorities having no further use for them. They were increasingly used as stimulants and euphoriants, especially after 1948. Laws were passed (see below) in 1949, 1951, 1954, and 1955 to control sale and supply but, by 1954, over ten thousand people had been found guilty of offences under them. Slightly more than half of these offenders were considered to be addicts. Responsible estimates of the number of people in Japan taking amphetamine for non-therapeutic purposes varied between half a million and a million and a half. In one town, Kurume, with a population of 90,000, there were approximately a thousand addicts; in a high school with 500 pupils, 4 per cent were thought to be addicted. Two Osaka psychiatrists had, between them, seen 599 cases by whom methylamphetamine was being used non-therapeutically during the period 1949 to 1953. Another Japanese psychiatrist reported on 492 cases of methylamphetamine psychosis. The majority of persons dependent on amphetamine

were men of social class V 70, per cent between 18 and 23 years of age. In the Kurume series, 26 per cent were unemployed. In the large Osaka series, 90 per cent were men and 45 per cent of these were unemployed. The commonest method of taking the amphetamine was by intravenous injection, working up from about 5 mg per day to a maximum of 600 mg per day within about four months; the majority, however, did not reach as high a dosage as that. The exact amount used remained rather uncertain, because the drug was manufactured illegally and addicts' statements could not be assumed to be truthful. A survey in 1951–52 indicated that 6 per cent of the illegally manufactured preparations did not contain amphetamine at all. Numerous cases of psychotic change were seen in the Japanese addicts. The clinical picture approximated to that of schizophrenia in a high proportion of these patients: blocking and other disorders of thinking, delusions and ideas of reference were common, but ideas of grandeur were rare. Depersonalisation and anancastic features were seen in the earlier stages. In 50 per cent of the patients there were acoustic hallucinations as well as somatic complaints of electrical stimulation, etc. There was lack of spontaneity, much irritation and anxiety, restlessness and, occasionally, tendency to violence. Depression and catatonic excitement as well as stupors were seen. Among the 599 patients investigated by Sano and Nagasaka there were 45 per cent in whom the illness took a schizophrenic form, 40 per cent in whom there were mixed manic depressive and schizophrenic features, 5 per cent with manic or depressive changes of effect and 10 per cent with apathy and semi-stupor. Although the clinical picture approximated to schizophrenia in 70 and 80 per cent, autism and lack of rapport were not observed. No physical signs were noted after withdrawal and there was quick recovery, so that in three weeks time 60 to 70 per cent of the patients were physically and mentally normal, and after six months 90 per cent of all patients were free of symptoms. Sano came to the conclusion that among those who had been taking amphetamines over a long period, 22 per cent had no psychotic symptoms, 62 per cent did become psychotic but quickly recovered on withdrawal from the drug, and 10 per cent developed psychotic symptoms which did not disappear on withdrawal. Another Japanese psychiatrist, Tatetsu, reported observations in Tokyo; he studied 492 cases of what he considered to be methylamphetamine psychosis; of these 36 per cent had a good remission and 37 per cent had a moderate remission. Japanese observers, like those in the United States, Great Britain and other European countries stress the frequency of relapse into renewed amphetamine consumption after the patient has left hospital.

In Sweden there was a similar outburst of amphetamine taking which began in 1938 and in the succeeding five years the sale of the drug increased twenty-fold, with high prevalence in large cities and university towns. It was then estimated that 3 per cent of adult population was using the drug although, of these, two-thirds did so only occasionally. The remaining third were regular users of phenmetrazine over a very wide range of doses and frequency. In 1943 the dangers were much publicised, with a consequent decline (40–60 per cent) in sales. Nevertheless widespread use continued and, in 1958, there was a further rise in consumption, especially by young men of the 20 to 30 year age group with criminal backgrounds.

Effects of continued misuse

It is possible to take amphetamines over prolonged periods for therapeutic purposes without developing signs of intoxication. There are, however, many reports of incontestable disturbance directly attributable to the consumption of these stimulant drugs. Moderate disturbance of this sort takes the form of irritability, sleeplessness, loss of appetite, agitation and depression; thus, a man who worked a 200-ton crane and who used benzedrine inhalers for nasal congestion found that he was getting dizzy, irritable and unsteady so that he was a danger at his work; the symptoms all disappeared when he stopped using the inhalers.

Similar, but more severe, disturbances arise from the grosser non-therapeutic consumption of amphetamines. In California, for example, the men attending a rehabilitation centre had been taking 20 to 40 mg three or four times a day intravenously, and more than this in some cases. Psychopathic traits were intensified, tension mounted and paranoid attitudes developed during the three to six days when the men were continuously awake; they were intensely preoccupied with their thoughts and activities, and talked incessantly. Many persons who have received amphetamine have enhanced sexual interest and libido, with some regression towards perverse forms of overt sexual behaviour.

Psychoses due to misuse

Psychoses due to amphetamine have been reported since 1938. A causal relation was disputed by some, until established by Connell in 1958. They have mostly taken the form of a paranoid condition with auditory and visual hallucinations in a state of clear consciousness; the similarity to paranoid schizophrenia may be so close that an erroneous diagnosis is easily made and the toxic nature of the condition passes unrecognised. A confirmed history of amphetamine consumption and disappearance of the psychosis within a week of discontinuing the drug are satisfactory criteria for diagnosis of the condition. A proportion of those who take amphetamine regularly have been doing so in order to relieve a psychiatric condition and may be practising self-medication. In such cases a psychosis which is provoked by amphetamine may show features attributable to the original mental disorder. Although the typical clinical picture may appear after only a single or a few doses of amphetamine given to a highly susceptible individual, it is commonly the outcome of prolonged intake or of a much larger dose than usual. The commonest dose producing psychosis in a series of patients was found to be in the neighbourhood of 325 mg though quantities five times as great have been taken before the psychosis appeared.

After a large dose, besides paranoid hallucinosis, there may be disorientation producing a clinical picture of delirium, but this is uncommon. So also is amnesia, but there is a report of a man who had been in the habit of taking amphetamine and on one occasion consumed approximately 1,250 mg during forty-eight hours; he injured himself by jumping through a window and, after recovering, could not remember what had happened. Some observers report depression as well as suspiciousness and the general paraphrenic syndrome. French psychiatrists have described a "pseudo-amphetamine psychosis" in which the patient has begun taking amphetamine in order to relieve difficulties in thinking and concentrating which were symptoms of early schizophrenia; with-

drawal of the drug led to disappearance of the grosser symptoms but not of the thought disorder or of the incongruous affect. It is sometimes difficult ot determine how far the clinical psychotic picture is due to amphetamine and how far to other drugs with which it is being combined.

The dangers are not over when the patient has completely recovered from his psychosis. There is a strong tendency to relapse if, as commonly occurs, the patient resumes taking amphetamine when he is out of hospital. A few observers report neurasthenic symptoms persisting for many months after the drug has been stopped.

Amphetamine psychoses now occur with increasing frequency in women, some of whom have taken the drug in large doses for nine or ten years, chiefly in order to deal with obesity. This applies particularly to dexamphetamine, methylamphetamine and phenmetrazine in varying dosage. In a series of thirty-one patients with psychiatric disorder attributed to amphetamines, there were seventeen women, all of them with severe personality problems.

The reason why some patients develop psychoses after taking amphetamine in moderate therapeutic doses, while others do not do so after continued consumption of large doses intravenously as well as orally, is still obscure. Several writers believe that this moderate dose effect occurs in persons who have psychopathic traits, especially schizophrenic or paranoid tendencies, but such an assumption is not borne out by available data; some who have been psychiatrically normal develop psychoses while others with indisputable schizoid characteristics and tendency to ideas of reference do not. It is still impossible to foretell whether any individual patient for whom amphetamine is prescribed over a long period will become psychotic at any stage. In some cases it seems clear that the drug has activated pre-existing schizophrenic trends and in others that it has directly produced a paranoid hallucinosis, i.e. a toxic psychosis which is, nevertheless, atypical in that consciousness remains usually clear and the patient has no disorder of orientation or memory. No one has offered a plausible and well supported explanation for the fact that, providing there has been nothing of the kind after the first dose or the first few doses, it is, as a rule, only after taking the drug for a year or more that a toxic psychosis occurs. In 1959, phenmetrazine and methylphenidate were put on the National Narcotics Drug List; in 1965, phenmetrazine was completely prohibited. The route of ingestion was usually intravenous and a high incidence of associated infective hepatitis was reported, i.e. 275 cases in the first seven months of 1967 and a total of 712 in four years. Sepsis could also be severe in those taking amphetamines intravenously. Illicit supplies of amphetamine, especially phenmetrazine, are still being obtained in Sweden; the number of violations of the law against possessing amphetamines has risen. A current estimate of illegal consumption of phenmetrazine is between 20 and 40 million tablets a year.

Legislation in Japan and Sweden

Legal action to restrict the consumption of amphetamine has been taken in several countries, notably in Sweden and Japan.

Japan

After the war the availability of large quantities of amphetamine led to its widespread use as a stimulant so that in July 1948 the Government, felt obliged to take steps to restrict its sale and then its manufacture. These measures did not

have the desired effect nor did a request to the manufacturers to cease production. A law was therefore passed in June 1951 which only allowed the drug to be used for medical purposes and for research; persons who were to handle amphetamine had to be licensed. There was then some improvement but soon it was noted that there had been an increase in criminal actions by persons taking amphetamine and that underground production had led to the appearance on the drug on the black market. In June 1954 the law was revised to give powers to compel addicts to enter a mental hospital for treatment and the penalties were increased, so that the heaviest penalty, previously three years penal servitude, was increased to five years. For a second offence or for handling the drug for purposes of gain it was increased to seven years, with a maximum fine of £500 as the alternative. Again there was temporary improvement, but it was found necessary in August 1955 to amend the act further in order to extend the licensing system to cover raw materials and to restrict production of the drug in the whole of Japan to two manufacturers. Concurrently with these changes in the law, there were variations in the number of arrests for offences connected with this drug; there were 40,000 arrests in 1953, 55,000 in 1954, 30,000 in 1955, falling abruptly to 5,000 in 1956 and to a few hundred in 1957. There is no means of knowing how far this can be accounted for as a result of police action or inaction.

Sweden

The vogue of amphetamine taking began in the late 1930's so that, by 1942–43, there were about 200,000 people taking it, though only about 200 were regarded as doing so to excess. The Swedish Board of Health then required that the drug should be obtained only on prescription. By 1954 it seemed that there was an alarming amount of amphetamine being taken by the intravenous route among Stockholm adolescents. By 1958 this had become much more widespread and the amphetamines were then classed as narcotics and special measures were instituted to detect those who were consuming them. Nevertheless, the taking of amphetamine by the intravenous route continued to increase, and, in 1967, the Government's Advisory Committee on Drug Addiction proposed further changes in legislation and stricter enforcement. The available statistics do not permit any conclusion to be arrived at regarding the effect of the above legislation either on the intravenous or the oral taking of amphetamines. The problem is still a serious one in Sweden where the Advisory Committee on Drug Addiction estimates that there are now several thousand persons misusing amphetamine in Stockholm and that there are also considerable numbers of persons taking it intravenously in the Gotebourg area and in Malmo-Lund.

Among the further legal steps which the Swedish Advisory Committee on Drug Addiction proposed (with the proviso that drug abusers should not be "forced into criminality") were:—increasing the maximum penalty to four years of imprisonment; strengthening the official machinery from prosecution controlling the import and sale of injection syringes and needles; and registering all medical prescriptions.

These measures assume a programme for the active treatment of addicts and international control. The fact that central nervous system stimulants are not covered by international agreement is often a hindrance to effective cooperation in the control of misuse.

BARBITURATES

Clinical and Pharmacological Background

Since they were introduced into clinical practice in 1903, barbiturates have proved to be valuable drugs and have been very widely used with relatively few adverse effects.

The therapeutic uses of the barbiturates are well known and fully described. They include the relief of insomnia and anxiety, the treatment of epilepsy, the induction of anaesthesia, the maintenance of continuous narcosis and the production of abreaction. The doses and frequency of injection required for these purposes, if properly regulated, are not such as to produce either addiction or withdrawal symptoms that are clinically recognisable, but when large doses are taken frequently, or over a long period, it is quite otherwise, and then the dangers described by Isbell and others are real and serious. Harris Isbell, the outstanding authority on their misuse and dangers, and his colleagues at Lexington have declared that "the manifestations of chronic barbiturate intoxication are, in most ways, much more serious than those of addiction to morphine. Morphine causes much less impairment to mental ability and emotional control, and produces no motor inco-ordination. . . . Withdrawal of morphine is much less dangerous than is withdrawal of barbiturates."

Whether addiction, physical dependence and a withdrawal syndrome could occur with barbiturates was long the subject of a controversy which reached its height in the middle thirties when the risks of barbiturate intoxication were likewise vehemently debated. The fatal outcome of "*Veronal*" when taken in very large doses was reported fairly frequently within the first decade after its introduction; by 1918 the possible development of addiction to it was alleged. Willcox, who had been consistently stressing the dangers, declared in 1934 that "the actual danger to the public in this country at the present time from addiction to these drugs (barbiturates) is greater than that from any other group of drugs, even including the dangerous drugs which are controlled . . . by special Acts and Regulations". Gillespie, who took the opposite view, insisted that barbiturates were safe drugs and that "withdrawal of barbiturates is not accompanied by the distressing subjective results and objective manifestations that accompany withdrawal of alcohol or morphine". Gillespie did not refer to Pohlisch who, in 1928, had described features of the syndrome coming on after abrupt withdrawal.

In 1956, the United States Congress received a report from its Subcommittee on Narcotics stating that "there is divided opinion among medical experts as to the addictive and habit-forming potentialities of barbiturates. Some contend that barbiturates are just as addictive as are narcotics, others claim that they are not addictive but that they are habit-forming".

Acute intoxication

This is most commonly the outcome of a suicidal attempt. It is often maintained that some depressed persons, having taken a moderate dose of barbiturate, become muddled and forgetful and, still feeling depressed and sleepless, take more and more until they have consumed a dangerous or lethal quantity.

The signs of intoxication are drowsiness, agitation (especially in the elderly), intellectual impairment, emotional instability, slurred speech, inco-ordination, and staggering gait. Obviously symptoms are very like those of alcoholic intoxication. In some patients there may be irritability, aggressive behaviour, paranoid ideas, and self-injury. Coma may be the final stage reached. The severity of intoxication runs parallel with the serum barbiturate level. As the patient returns to clear consciousness, there may be a period of euphoria and of puerile conduct in which inhibitions lose their force; for this period there may be subsequent amnesia. Use of barbiturate intravenously to produce anaesthesia shows the phenomena of intoxication and recovery in concentrated and controlled form.

Psychological tests indicate that there is prolonged reaction time, impaired visual perception, and impaired attention for as long as fourteen hours after a single large dose. People already mentally abnormal may show anomalous response to barbiturates, e.g. a patient prone to manic-depressive illness became manic after a large dose.

Chronic intoxication

The main signs are similar to those of acute barbiturate intoxication, only milder. Besides confusion, defective judgment and loss of emotional control, there is accentuation of any defects in the patient's personality. He becomes slovenly in his dress, spills his food and may get annoyed at fancied insults. Signs of malfunction of the central nervous system occur which may be mistakenly attributed to cerebellar disease, disseminated sclerosis or alcoholism e.g. dysarthria, ataxia, hypotonia, tremor, and transient extensor plantar reflexes. Blood pressure and body temperature tend to fall. There is, however, considerable variation between individuals, and in the same individual at different times.

The motives that seem to determine habitual consumption of barbiturates are diverse e.g. to assist in bearing or relieving emotional distress, to counteract some of the stimulant effects of amphetamine, to reinforce or replace the action of alcohol or opiates, or to help in reducing insomnia. As a rule, barbiturates are taken in solitude rather than in company.

Writing in 1950, Isbell and his colleagues knew of no reports of pathological changes in the central nervous system in these patients. "If irreversible pathological changes occur in man, they are so slight as to be undetectable by clinical means and are not sufficient to cause any permanent physical handicap to individuals who have abused these drugs. Barbiturate addicts are much more likely to develop permanent damage as a result of trauma resulting from a fall while intoxicated, or from a convulsion during abstinence, than as a result of pathological changes due to direct effects of the drug". A German psychiatrist, however, found pathological changes in the putamen and the cortex as well as in the liver of a man of 53 who had been taking barbiturate in large doses for eleven years, but it is possible that the changes noted were an accompaniment of the very severe withdrawal syndrome through which the man passed before he died.

Tolerance

Tolerance develops but is less than in morphine addiction. Those addicted to barbiturates increase their dose only after some weeks or months and then by a

small amount. Tolerance is lost after a period of abstinence. Among barbiturate addicts there have been found some who developed confusion, vertigo and nystagmus if they were given small doses of thiopentone; a special sensitivity to barbiturate has been assumed in these persons.

Withdrawal syndrome

Abrupt withdrawal of barbiturates from a person who has been taking them to excess may bring on an alarming and sometimes a fatal sequence of events. From 1912 onwards, there had been reports, mainly in the German journals, of such consequences of abrupt withdrawal, but it was not possible to demonstrate conclusively the causal nexus because the statements of patients about the dose and frequency of administration were not reliable; the barbiturate was often mixed with other drugs which they had been taking, they were physically ill and under-nourished, and the withdrawal of the barbiturate was, in many cases, not abrupt.

Reports of convulsions and delirium after abrupt withdrawal appeared between 1939 and 1942, but their interpretation was somewhat equivocal, especially in the emotional atmosphere which then prevailed on this topic. However, the experiments of Isbell and his colleagues at Lexington, reported in 1954, removed all grounds for reasonable doubt and subsequent experiments by the same group provided further confirmation. Nevertheless, doctors went on prescribing barbiturates in doses which indicated the comforting notion that they were harmless sedatives and, in particular, the risks of abrupt withdrawal were often ignored. Thus, in Birmingham (1960), five chronic addicts were reported who had had their barbiturates so abruptly terminated that in four of them fits occurred and the fifth passed into delirium. In 1967 an article in the *Lancet* reported four instances of convulsions and other symptoms due to abrupt cessation of barbiturates. The author commented: "That abrupt withdrawal of barbiturate in addicts may be followed by fits seems little known outside neurological and psychiatric practice."

During the first twelve to sixteen hours of abstinence a patient may become apprehensive and weak but, as a rule, he reports improved well-being. Then anxiety comes on with headache and twitching, possibly vomiting, slight stimuli cause excessive response, he cannot sleep and, after twenty-four hours from the time of cessation of the drug, severe disturbance is obvious. Nausea and abdominal cramps then develop, pulse rate rises and, between the thirtieth and forty-eighth hour of withdrawal, convulsions indistinguishable from grand mal epilepsy are very likely to occur. There may be two or three of these convulsions, but very seldom more than four. Minor episodes of clonic twitching occur. Occasionally the convulsions may occur as early as the sixteenth hour after withdrawal or not until as late as the eighth day. At about the same time, or slightly later, a psychosis may develop which is very like delirium tremens except that there is a tendency to form delusions of a systematised kind and there is also some euphoria. The duration of the psychosis is not more than five days; it ends with prolonged sleep even though no treatment is given. The condition is normally self-limited but when the withdrawal symptoms are severe barbiturate must be given, if necessary, by the intravenous route.

The occurrence and severity of the withdrawal syndrome is closely related to

the dose which the addict has been taking. It is unlikely that there will be a withdrawal syndrome if the dose has been below 0·4 g per day. Other factors will be sex, age, body size, length of intoxication, physical state and personality. On the whole, a daily dose greater than 0·4 g of pentobarbitone, quinalbarbitone or other barbiturate is required to produce a clinically significant degree of physical dependence.

The likelihood of convulsions and delirium after abrupt withdrawal is high if the patient has been having a large dose of barbiturate beforehand for some time. This is well illustrated in a later study by Isbell and his colleagues in which nineteen subjects had quinalbarbitone six times a day by mouth in the highest dosage that was compatible with safe management. Though they differed widely in the amount that they were able to take, only three of the nineteen failed to show either convulsions or delirium or both; all but four of them had insomnia so that they slept two hours or less out of twenty-four hours, and one subject went without sleeping for eight consecutive days. In the sixteen patients who had convulsions they occurred 24 hours after the last dose of barbiturate in the earliest case, and after 115 hours in the latest. All but two of the thirty-three seizures collectively experienced by these patients occurred within 78 hours after withdrawal of the barbiturate. Twelve of the nineteen subjects developed delirium during which there was disorientation, visual hallucinosis and pyrexia.

In general it is agreed that people who consume 900 mg or more of these drugs daily are fairly certain to show symptoms of abrupt withdrawal; no such effects will be observed in people who have been consuming up to 200 mg or more of these drugs each night. Before arranging the details of deliberate withdrawal it is important, because of the risks, to determine, if necessary by means of a test dose, whether the intoxicated patient has been a chronic addict. If it is clear that he has become physically dependent on barbiturate then he should be given approximately 800 mg pentobarbitone divided into four doses during the first day; subsequently the total of the four daily doses should be reduced by 100 mg a day, or, if he has a convulsion, by only 50 mg a day. If his degree of tolerance suggests that he is physically dependent to a marked extent, then he might begin on 1200 mg, divided into four or six doses, every twenty-four hours. Allowing for wide personal differences, 800 mg and eight weeks can be regarded as the approximately daily dose and duration necessary for the development of physiological dependence.

Risk of death

In spite of the relatively low mortality rate, which averages about 8 per cent, barbiturates cause more deaths than any other solid or liquid poison in the United States. Death from poisoning may occur either as the result of a very large single dose of barbiturate or of several fairly large doses taken in quick succession. Death may also result from abrupt withdrawal. Sometimes in fatal cases the barbiturates have been taken together with other drugs such as alcohol and opiates. Some of the apparent suicides may be due to impairment of judgment and memory so that the patient has not realised how many capsules he has taken and keeps on taking more. The lethal dose of barbiturate has been stated to be about 10 grammes though a bigger dose than this has been successfully survived; conversely, death has occurred from broncho-pneumonia after the

patient has taken no more than 4 to 8 grammes of barbiturate. Status epilepticus has been stated to occur before death.

The risks of the withdrawal syndrome are greatly increased when the patient conceals the fact that he has been taking barbiturate as well as opiate in large quantities. French authors describe a case in which the withdrawal syndrome was characterised by epileptic seizures of the focal type with rotation of the head and eyes to the right and tonic spasm. There were four such attacks, which ceased when the patient was given barbitone. However, on the following day death occurred suddenly from pulmonary embolism. At post mortem there were extensive changes in the amygdala and the striate body as well as in the cerebral cortex. It was concluded that these recent changes in the central nervous system were a consequence of the withdrawal syndrome and particularly of the epileptic seizures.

Other risks

Barbiturates may precipitate an attack of acute porphyria in a predisposed person.

In newborn infants whose mothers had received barbiturate just before delivery there was diminished attentiveness at two to four days of age and belated adjustment to breast feeding.

Driving a motor car may present some risk. Those who take a hypnotic dose of barbiturate cannot safely drive, but those who take only a mild sedative dose may do so without danger. The guide issued by the American Medical Association stated that "a barbiturate addict is incapable of driving a motor vehicle safely". In Ontario in 1950, only one person was detected driving a motor vehicle while under the influence of a drug, but in 1964 twenty-five such cases were recorded in eighteen of whom barbiturates were detected in the blood or other body fluids.

Synergistic combination with other drugs

In the United States, and to some extent in the United Kingdom, barbiturates are often taken at the same time as other drugs, especially alcohol or amphetamine. A proprietary combination of amylobarbitone with amphetamine "*Drinamyl*" has been popular and misused in both countries. Whether the action of alcohol upon barbiturate is only additively synergistic or whether it is potentiating is uncertain. The risks of driving a motor car are greatly increased if the driver has taken barbiturate as well as alcohol.

Cocaine users are alleged to combine barbiturate with intravenous cocaine in order to reduce the anxiety and emotional tension produced by the cocaine. A different sort of combination, intended to make barbiturate less dangerous, is with bemegride for the purpose of preventing terminal or prolonged sleep from overdosage; the efficacy of this combination for this purpose is to be doubted.

Addiction

Prevalence

The numbers of people who take barbiturates regularly or to excess are not known. There are, however, data on some associated aspects. In 1962, there were

1,476 deaths in England and Wales due to barbiturate poisoning; 1,083 of these were suicides and 393 accidents. There had been a very rapid increase in such deaths during the previous decade. Thus, whereas during 1941 to 1950 the average annual number of suicides from barbiturates was 104, for the five years, 1958 to 1962, it was 735, and the corresponding rise in the numbers of accidental deaths from barbiturates poisoning was from 60 to 285 in the same time interval.

Of all people aged 15 and over who died from all causes in England and Wales in 1962, barbiturates killed 1 in 441 men, and 1 in 306 women. The highest suicide rate for barbiturate poisoning was in women aged 45 to 64. Taking into account known cases of attempted suicide by barbiturate and patients treated for barbiturate poisoning in general hospitals, it has been estimated that approximately 110,000 cases of barbiturate poisoning occurred in 1959.

The quantity of barbiturate prescribed annually by general practitioners in the National Health Service doubled between 1953 and 1959, i.e. from 81,000 to 162,000 lbs.

In Switzerland the consumption of barbiturate has declined since tranquillizers were introduced into therapeutic practice, but this decline is in contrast to what has been observed in England and the United States.

Recognition

A 200 mg dose of pentobarbitone "*Nembutal*" is given by mouth. If, after an hour, the patient is asleep, or intoxicated (as shown by nystagmus, ataxia, slurred speech, etc.) it is inferred that he is not physically dependent on barbiturates, whereas if he has been taking them to excess for some time he will have developed tolerance and he will not be intoxicated by such a dose. If he has evidently acquired tolerance the procedure may be prolonged by further doses until there are signs of intoxication. The findings act as a guide to dosage during deliberate withdrawal.

Prevention

There is abundant evidence that doctors prescribe barbiturates in large quantities without very much regard for the risks which attend their use. There are strong grounds for insisting that prescriptions should be limited in the amount made available and that a "refill" should require a new prescription. Emphatic advice to this effect was put forward by the American Medical Association in 1965. They also deprecated prescribing barbiturate for narcotic addicts, sociopaths and alcoholics, and they reiterated that to drive a car while definitely under the influence of barbiturate is to run a considerable risk of accident. Lately the somewhat extreme view that possession of barbiturate should be made a criminal offence has been put forward. However, it will do us little good if, because of the growing reports of their dangers, barbiturates fall into disrepute as did the bromides, only to be replaced with other equally harmful and probably less beneficial drugs.

The Commission on Narcotic Drugs at their Seventeenth Session adopted a resolution recommending that governments should take appropriate steps to place the production, distribution and use of barbiturates under strict control.

Effects on Mentally Normal Persons

The effects of LSD on mentally normal persons can be divided into direct (or pharmacological) effects and indirect (or secondary) effects. Personal variations are considerable in the former but incomparably more so in the latter. The direct effects are, to some extent, specific; the indirect reflect the personality and interests of the individual.

The direct effects are chiefly either autonomic, such as nausea, loss of appetite, dizziness, paresthesiae (especially of the face), weakness, anxiety, trembling, sweating, dilated pupils, rise in blood pressure, muscle tension and inco-ordination or perceptual, e.g. undulation of surfaces and outlines, intense luminosity of colours, distortion of perspective, anomalies of space perception and of body schema (including depersonalization), disorder of thought, lack of appreciation of the passage of time and change of mood.

The indirect effects, which are remarkably varied, depend much more on the intoxicated individual than on the intoxicating drug. LSD facilitates these effects (just as a sedative can create the conditions preliminary to a vivid and eventful dream), but it is not essential for their occurrence. Hallucinations, in the strict sense of the word, do not occur, but the specific perceptual disturbance may be worked up by imagination into a very complicated visual and emotional experience, difficult to communicate and rapidly changing. Some who have had such an experience report that it requires a lot of "mental energy" and was hard work which they would not wish to repeat. Others describe orgiastic, euphoric, mystical and ecstatic states. Usually the most evidently stable have been disappointed in not acquiring transcendental knowledge or an *au-delà* feeling as promised by Aldous Huxley, Dr Leary and other enthusiasts.

There is universal agreement that the secondary effects of LSD depend a great deal on the situation in which it is taken, the expectation of the taker (and of the person who is giving him the drug), his personality and background, and his social and cultural setting. If the source of the drug is illicit, and the setting is one in which the aim is to get high with a group of young people, then the effects will be similar to those achieved with the use of various other substances—orgiastic, artistic or euphoric. On the other hand if the drug is taken in a medical setting the responses are more likely to be in the area of changed perspectives and integrated experiences.

No account of what it was like to have had LSD is too highly coloured to be credible, granted the requisite psychological and social context; and none is too jejune and dry, with the same qualification. Accounts which read like fluent extravaganzas, e.g. some of those set out at length in Masters and Houston's recent book, are at the other extreme from the sober reports by people like Raymond Mortimer or those of the patients gravely ill with cancer whom Eric Kast studied. Most of the takers reported both pleasant and unpleasant effects, as well as changes in their feelings towards others and their attitudes to themselves. But "one person taking about 200 micrograms became psychotic, another also taking 200 micrograms claimed only that his eyes were blurred". In some

studies, but not in all, a larger dose meant a more severe reaction, chiefly evident in the direct effects of the drug.

In a study of 30 Japanese students who had been carefully selected for normality, a dose of 1 microgram per kilogram by mouth produced undulatory visual phenomena but little else. With double this dose things looked flat or blurred, time sense was altered, and there were changes in bodily feeling. The same dose, given intramuscularly, evoked visual hallucinations, abnormal psychomotor activity, ideas of reference and a sense of super-human powers. Two of the subjects became so acutely agitated that they had to be in hospital for the next twenty-four hours.

Very large doses by mouth have brought about gross neurological disturbances. A man who doubled the dose on successive days, so that by the fifth day he was taking 4,000 micrograms, had slurred speech and ataxia. But these symptoms of gross or chronic intoxication are not commonly seen because such large doses are not taken and tolerance develops fairly rapidly.

Supposed psychotic effects

LSD and mescaline were formerly called psychotomimetic drugs because they so often produced psychological disturbances very like those of the psychoses. So far as this referred to "exogenous" psychoses, i.e. those produced by toxic and other external interference, it was a legitimate term. But in practice it was often asserted or assumed that the symptoms of schizophrenia could be reproduced or mimicked by LSD and mescaline. This is incorrect. Perceptual disorders caused by LSD are predominantly visual, whereas those of schizophrenia are predominantly auditory; thought disorder in schizophrenia has features not mirrored in LSD poisoning; consciousness is restricted or blurred by LSD but not, as a rule, in schizophrenia. Some of the more dramatic reports of experience under LSD are like those of hysterical fantasy (or the productions of a patient receiving treatment on the lines of C. G. Jung's *Analytical Psychology*) far more than they are like those of schizophrenia.

Effects shown by psychological tests

Clinical observations have been largely concerned with the subject's account of his subjective experience and have not been checked, except in very rare instances, by comparison with the reported experiences of persons similarly selected, indoctrinated and expectant, who have not had LSD but have been given a placebo or a non-hallucinogen. Controlled psychological tests have provided more objective information; there is now a fairly large number of these available.

During LSD intoxication psychological tests show impairment of intellectual functions, such as abstract reasoning, memory, planning capacity, awareness of body image, fluency and comprehensibility. Some other cognitive functions are impaired, as are spatial and other forms of perception, expecially those with a visual component. Suggestibility is heightened.

Two psychological studies, though provisional and inconclusive, point in a more favourable direction than the foregoing. One of these found that tests carried out before the fifteen subjects had had LSD (200 micrograms by mouth), and repeated a week after they had had it, indicated a decrease in anxiety,

dogmatism and aggressiveness of the paranoid sort. The other study was on the effects of mescaline, not on those of LSD, but these two drugs have such similar psychological effects that the reported observations are relevant here. Twenty-seven workers in professional fields were asked to solve problems before, during and after receiving a single dose of mescaline; the findings suggested that, under carefully organized conditions designed to allay fears and expectations of extraordinary happenings, the drug facilitated the solving of problems and that this heightened ability might continue for some weeks after the drug had been taken; the authors stress that this was only a pilot inquiry.

Thirty-one men were given a battery of tests which were designed to estimate their "creative" processes before and after receiving LSD. The outcome of the tests did not suggest that LSD enhances "creativity".

Apart from these tentative reports, psychological tests have shown that the effect of LSD is to reduce psychological functional efficiency. These results are in striking contrast to the heightened awareness and enhanced understanding reported in the subjective accounts of some addicts.

Effects on Mental Patients

Many studies of the effects of LSD have been carried out on a very mixed assembly of schizophrenics, depressives, neurotics, delinquents and normals. It is often impossible, in these studies, to differentiate the effects of LSD from the phenomena of pre-existing illness.

Much attention has been paid to the action of LSD on chronic schizophrenic patients. There is evidence from controlled studies that these patients respond less to the drug than normal people do and that they persist with conditioned responses longer than normals after the rewards have been withdrawn. Persons with schizoid personality have, however, been reported who developed a full-blown schizophrenic illness after taking the drug. Difficulties of interpretation are illustrated in a case reported by Charles Savage: he gave a girl LSD weekly "to reorganise her equilibrium" but it "shattered her defences" and she threw herself under a train; "LSD mobilised her feelings and affects which had been successfully handled by nihilistic delusions; it also mobilised the supreme resistance, suicide".

The intensification of existent neurotic disorders which a single dose of the drug brings about temporarily makes it important to find out, if possible, how far vulnerable people take it regularly without any medical supervision. The evidence is discrepant, and varies according to whether the investigator made his inquiries among professional and other adults who expected to achieve greater understanding, or among young people who were drifting and looking for stimulation.

In the professional group studied by Richard Blum, those who had taken the drug when it was offered them were compared with others who had refused it in similar circumstances. The former were more often single, religiously active men who were dissatisfied with themselves and had tried other drugs such as marihuana, mescaline and methedrine but "no important differences in ego control, trust and gross personality disorder were observed". Blum adds in a footnote that "the mere presence of prior personality pathology does not predict LSD

psychosis" for which he calculates a minimal 2 per cent risk among LSD takers. He found that husbands persuaded their wives to join them in taking the drug; if the wife refused, divorce followed.

Two other investigators (Ludwig and Levine) collected their data from in-patients at the Addiction Centre at Lexington. They recognised three groups of LSD users: firstly addicts who also take narcotic drugs, secondly, would-be artists and rebels who also may take hashish or amphetamine and are searching for something to rouse them from apathy, overcome social inhibitions and "make life more meaningful", and, thirdly, a small group of people who take the drug to attain a personal esoteric goal—"greater insight, fuller consciousness, fusion with nature, creativity".

Another inquiry, carried out on in-patients, showed the LSD users to be scholastic failures with bad occupational and social records resulting from schizoid, depressive or hysterical personalities and habitual use of more than one drug that, in many cases, had been going on for several years.

The personality and attitudes of twenty-four graduate students who volunteered for an experiment without knowing that LSD was involved were investigated and compared with those of two control groups. Those among them who responded intensely to the experience tended to prefer more unstructured spontaneous introspective life and scored higher on tests of aesthetic sensitivity and imaginativeness than those who had no taste for the experience and tended to respond minimally to it. After six months 58 per cent of them subjectively reported a lasting effect, but attempts to measure these changes by means of psychological tests provided only minimal evidence in support of this claim.

The longing for a "psychedelic" transformation is often expressed by the addict in religious or mystical terms. "A psychological death and rebirth experience" after which he "rejoins the human race"; it equips him with a new value system and brings him "face to face with the universe". The language used to describe this is largely taken from Buddhist writings. At the Psychedelic Training Centre, passages from the Tibetan Book of the Dead are read by the postulant before he takes LSD and later are again read aloud to him by his companions.

Use in Psychiatric Treatment

In the numerous papers on the use of LSD as a treatment there is much variety in dosage, mode and frequency of administration, choice of patients, and results. There are flat contradictions; some find that the patients who respond best to LSD are those with obsessive neurosis or character disorder or sexual perversion; others report that it is just these groups of patients who are least suited to LSD treatment. There is no common form of mental disorder which has not been claimed by somebody as likely to be benefited by LSD, the treatment being in skilled hands, of course. The nearest approach to agreement is in excluding hysteria and in emphasising that LSD is ineffectual except as an adjunct or preliminary to psychological treatment either given in a group or individually. A great deal of ingenuity and experience has gone into the evaluation of results and towards explaining why the treatment should be beneficial; but it is impossible to draw any firm conclusion about the efficacy of LSD either because it was not employed alone, or the experiment was uncontrolled, or the treatment was

practised on patients with illnesses the course of which, apart from treatment, is extremely variable. An unfavourable outcome of LSD treatment can quite well be attributed to constitutional disease (as when a patient who had previous attacks of depressive psychosis developed another severe attack during LSD therapy) and, when the outcome is favourable, the same uncertainty prevails.

The general impression made by the reported studies is of unconfirmed success, but the evidence is inconclusive and the outcome of LSD treatment must be regarded as unpredictable. The situation is very like that which has long characterized efforts to evaluate psychotherapy, and, since patients who are treated with LSD are almost always given psychotherapy as well, the uncertainties are compounded.

The disorders which have received most attention, or on which controlled observations have been made are alcoholism, character neuroses, and sexual perversions.

In the treatment of alcoholism, the most successful results have come from workers in Saskatchewan; they report abstinence from alcohol ensuing on the use of LSD in a third or more of the alcoholics treated, and a close relation between such sobriety and the new way of looking at life which was brought about by the LSD experience. Furthermore, they found that improvement noted immediately after the treatment tended to be maintained. However, another group of investigators, which included a former leader of the Saskatchewan workers, reported in 1966 from New Jersey that they had carried out a controlled follow-up study in which twenty-eight alcoholic patients treated with LSD were compared with thirty-four alcoholics who received standard non-LSD treatment. They found that improvement reported by the patients immediately after either form of treatment had no relation to the later outcome. Thus, although the LSD group at three-months' follow-up showed a much greater improvement than the comparison group, after six months and twelve months this advantage had considerably lessened. The wives of the LSD treated patients were correspondingly disillusioned.

Other Canadian studies, which were mostly enthusiastic a few years ago, are now less so or even sceptical. A report from Toronto comes from two investigators (Smart and Storm) who, in 1964, reviewed the situation and found that no report then available met the basic requirements for a valid study of the therapeutic effects of a drug. In 1966, the same investigators reported a carefully controlled study of chronic alcoholics treated with LSD in which control groups received either ephedrine sulphate instead of LSD or no drug at all but only the general treatment of the clinic, which the other two groups also received. All three groups showed improvement during the first six months after treatment, but without significant differences between the three groups. The authors concluded that "lysergide . . . failed as an effective adjunct to psychotherapy, in contrast to the claims made in previous studies".

Combination of LSD with psychotherapy

Those who have treated neurotic patients with LSD have aimed at facilitating the task of psychotherapy by abreaction, thus either bringing repressed material into consciousness and communication or providing the self-revealing "psychedelic" experience which refashions psychic life. Far-fetched material, e.g. literal reproduction of being born, is taken at face value and the language is high flown;

as a Scandinavian psychiatrist puts it, "contrasted with cosmical experience (effected through LSD), with an understanding of deeper reality and meaning in life, the many analytical problems seem a trifle. Patients who, previously, have gone to analysis for a long time in vain have, face to face with the universe and the higher powers, managed to look at their own problems at a distance". The recorded results of the LSD treatment of neurosis are not convincing, in spite of the manifest enthusiasm of many of those who have conducted such treatment on a large scale. Others, however, are less satisfied with the results: one of them (Robinson) concluded that "we have no evidence that LSD has a greater value than other drugs".

It is impossible to reconcile these results with those of an Australian psychiatrist who obtained 47 per cent of successes with LSD as the adjunct to psychotherapy as against 12 per cent in a comparable group who did not have LSD but only psychotherapy; methodologically, however, this study left much to be desired.

A Czech study, evidently less open to this objection, yielded better results from LSD (100 micrograms) given in individual sessions, than were obtained from a control group who had no LSD, but the control group did better than a group who had a smaller dose of LSD (50 micrograms in each session); the number of neurotic patients in the groups was, however, small—eleven or less, and the outcome of treatment was assessed solely from the patients' replies to a questionnaire.

Invariably, in the reported experiments with LSD treatment, the drug has been an adjunct or accompaniment to some form of psychological treatment. One combination from which its proponents report considerable benefit is of hypnosis and LSD. This combined procedure is designed to bring about an altered state of consciousness from which the patient emerges with a feeling of rebirth or rejuvenation, in which he understands the dynamic reasons for his behaviour; "almost any theoretical orientation would prove equally effective, provided that the theoretical framework be internally consistent, fit in with the patient and the therapist". In their most recent report the chief proponents say that a single "hypnodelic" treatment can effect dramatic relief of symptoms and constructive changes in attitude, but they do not know how long these will last or which patients are most suitable for the treatment.

The combination of LSD with group psychotherapy is strongly advocated by some, including English and Scandinavian psychiatrists, though the diversity of procedure adopted and other handicaps to evaluation are, as usual, prominent. Group experiments have been conducted in such a way that they provided data on the effect of LSD upon social interaction. In one study signs of tension, overt hostility and disagreement increased, though they were not recognized as such by the intoxicated subjects. In another the subjects (university students) were found to be more active and aggressive under the influence of LSD; they attempted fewer solutions to problems set them as joint exercises and they exchanged less information; they were also less accurate in perceiving other people's attitudes towards them.

Use in children

There is surprisingly little sign in the literature of LSD that the drug is re-

garded as unfit for children. Richard Blum reports that in the professional group whom he studied "there are also cases in this sample where parents have initiated their children (into the use of the drug), but these have always been young children (pre-teenage) and young parents (pre-forty)". Several users "had introduced their parents to LSD and their younger teenage bortohers and sisters to 'pot' (cannabis), or peyote (mescaline). In this professional group, wives had to take drugs as a test of virtue and loyalty, and there was pride when a father or an aunt could be persuaded to join in the inner circle. Similarly, approval was forthcoming when young relatives began to use drugs spontaneously; "I was really pleased when Kate came up from high school one night and told us she'd been turned on to 'pot'. Imagine, only fourteen, and so mature and sophisticated!"

Although it is widely assumed and affirmed that in schizophrenic patients LSD can intensify the psychotic symptoms, it has been used since 1961 to treat schizophrenia in children. Lauretta Bender, a very prominent expert in child psychiatry, has treated fifty-four schizophrenic children, aged between 6 and 15 years, with doses of 100 to 150 micrograms daily for from two to eighteen months. She was aware of the risks; "because of the rather violent psychotic reactions described when adults were given large doses of LSD we were extremely cautious when first using the drug, even obtaining parents' consent. We soon observed, however, that the children showed no serious side-effects, no evidence of severe disturbances". After LSD the schizophrenic children in the sample who showed the autistic syndrome, especially if they had not reached puberty, became less anxious, more aware and responsive and more socially mature, while their speech improved. The other schizophrenic children, who were not initially mute and withdrawn, became less prone to take flight into fantasy and showed better grasp of reality after having had LSD; thus, some became depressed because of realistic recognition of their personal problems.

In another New York experiment twelve autistic children, aged from five to eleven years, showed physical and psychological effects during the ensuing four hours after receiving 100 or 200 micrograms of LSD; the effects varied much from child to child and did not include better verbal communication. Still another New York group saw no improvement in a child aged eleven to whom they gave LSD on twenty-eight occasions. A Los Angeles group gave 50 micrograms of LSD to a pair of identical autistic twins aged five years, and observed temporary benefit in that there was more "eye to face contact", more laughter and smiling, and some movement towards the investigator.

The evidence of improvement adduced in these reports does not seem enough to justify continuing to give so potentially dangerous a drug to young children.

The psychotherapist who uses LSD

It is frequently emphasized that the therapist who uses LSD should himself have had it so that he can better enter into the reported experiences of the people he treats. This copies the argument that those who practise psychoanalysis should themselves have been psychoanlaysed and carries with it the probability that the outlook and observations of the LSD therapist may not be reliably objective. Ditman and his colleagues in Los Angeles, who made a special inquiry into the kind of subjects who reported "claimed" improvement after LSD,

concluded that "perhaps LSD is unique in that it prompts to many claims (of improvement), not only from (normal) subjects, and patients, but from investigators themselves". Imperfect memory and selective recall can play a large part here.

Adverse Effects

Harmful mental states attributed to LSD have often been described. Some of them occur during the period of intoxication, others when the direct effects of the drug have ceased to be evident.

During the first few hours after taking the drug there may be violent behaviour; a panic-stricken or paranoid patient may attack other people because he believes they threaten him, or he may hurt himself by smashing things or, for example, by pushing his hands through glass; some, if they were not restrained, would kill themselves, either because they have developed a depressive self-hatred in the period of intoxication, or because they have a feeling of superior power and invulnerability so that, for example, they think they could fly from an upper window. How frequently this sort of behaviour occurs depends *inter alia* on the circumstances in which the drug is taken. Whether it depends also on the dose given is a matter about which there is no unanimity.

Many of the acute effects of intoxication by LSD are akin to the phenomena seen in mental disorders, so much so that there has been much controversy as to whether they are to be regarded as exogenous, i.e. toxic disturbances attributable to the extrinsic agent, or, on the other hand, are so close to the clinical phenomena of schizophrenia that they throw light on the genesis and pathology of that disease. When the effects clear up within twenty-four hours of taking the drug they are not usually regarded as harmful. There are, however, patients in whom these acute effects shade off into more lasting disturbances. The chief morbid features that persist in this way are depersonalization, visual hallucinations and other disorders of perception, anxiety, depression, cyclothymia, and paranoid attitudes and beliefs. They may last only for a few days, may be continued for months, or may develop into a chronic condition.

It is, at present, quite impossible to tell how frequently these dangerous reactions occur. In more than thirty papers, psychiatrists have communicated details of untoward reactions; some of them have seen only one such affected patient, others have seen three or four. But it cannot be assumed that most of the patients who have untoward reactions are seen by psychiatrists or by doctors, or that the doctors who do see them would report them in articles in the journals. Moreover, the number of persons who take LSD is quite unknown and, consequently, the frequency of adverse reactions cannot be measured. However, some notion of the position can be gathered from approximate figures supplied by North American investigators.

Forty-four doctors who had published papers on LSD replied to an inquiry regarding adverse reactions which they had encountered. Their answers covered about five thousand persons of whom some had had the drug as part of their psychiatric treatment and others had had it given them for experimental purposes. Of the former 0·18 per cent developed a psychotic aftermath, but fewer (0·08 per cent) of the experimental subjects did so.

A group of psychiatrists working in the Medical Centre of the University of California at Los Angeles had, during the eight months between September 1965 and April 1966, given psychiatric help for LSD reactions to between five and fifteen persons per month. The total number of persons they saw on this account was seventy, constituting 12 per cent of all patients who attended the Centre in the Emergency Service. Twenty of them were seen because of persistent hallucinations, seventeen because of anxiety, fifteen for depression and fourteen for confusion. Five of them had attempted suicide; ten of them were paranoid, twenty-five had to be admitted to hospital as in-patients and, of these, all but seven had to stay in hospital for more than a month, sometimes for a matter of three to five months. It is difficult to say whether these were typical groups of LSD takers, though most were young men, unemployed or students; a third of them had also used cannabis during the previous six weeks and eight others had used amphetamine; four had used heroin and barbiturates. Thirty-three had not taken any drug but LSD. They were not, however, a mentally healthy group; the majority had had previous psychiatric attention. Nine had been before the courts for various offences. The psychiatrists reporting this series are convinced that there are many adverse reactions to LSD which do not come under medical notice, especially those which subside after a few days or weeks.

A Canadian series of 150 patients treated with intramuscular LSD included four who became psychotic and had to be treated with electro-convulsive therapy on that account. A New York series included sixty-five patients who had taken LSD and had entered hospital during the ensuing ten months, chiefly because of panic reactions, overt psychosis, or recurrent distressing symptons. Of sixty-five patients in a German series treated with LSD, two developed serious symptoms.

A disconcerting late effect of LSD intoxication is the recurrence of visual hallucinations and other symptoms weeks or months after the last administration of the drug. This can be very alarming to the patient and, because of the visual perceptual anomalies that occur, or the depersonalization, it may interfere with his work. In a few such cases auditory hallucinations or catatonic symptoms have recurred.

Physical ill effects are apparently rare. Fits have been reported but so infrequently that the data cannot be assessed. A man aged 31 took a very large dose (5 milligrams) of LSD by mouth and, when admitted to hospital, he was incoherent and required intensive treatment. Another patient, recorded in France, gave himself a large dose of LSD intravenously, and passed into a coma; he also required intensive treatment.

It is clear that an appreciable number of those who take LSD develop harmful reactions, either during the period of intoxication or afterwards. In most cases these are transitory disturbances, but they may lead to suicide or, as in at least one reported case, to homicide. It is, however, by no means clear what part LSD plays in bringing about these disturbances. Nearly all the people affected have, according to retrospective accounts, been mentally unstable before they took the LSD; some of them were under treatment for neurotic disabilities, psychoses, or character anomalies, and others had drifted from one failure to another. They had mostly obtained their LSD through illicit channels and it is possible that the drug was contaminated, though this seems an unlikely explanation in view of the similarity of the adverse reactions reported from very diverse countries (e.g. Japan and Czechoslovakia). It may be fairly concluded that adolescents and

young adults who are psychologically and socially unstable and take LSD stand in the most danger of harmful reactions, though these also occur in patients who receive it from psychiatrists who find LSD valuable in treatment.

The difficulties are illustrated by a Danish woman aged 25 who killed her lover. She had become depressed and received five LSD treatments, the first four with a week's interval between each, the last after a two-week interval. During the period in question, she made several attempts at suicide but improved sufficiently to be discharged from hospital. On the day of discharge, three days after her last LSD treatment, she went to her lover's place of work and stabbed him fatally. On the psychiatric evidence it was concluded that LSD had activated already-existing impulses and had weakened inhibition and self-control.

In a study directed at clarifying this aetiological question, twenty patients admitted to a psychiatric centre, who had taken LSD at least once, were compared with similarly admitted psychiatric patients who had not had LSD. The LSD group had a much worse work history than the others; they were drifters—two were male prostitutes, one was a thief. All but two of the LSD patients had taken other drugs, often over a period of years. Twelve of the twenty had taken marihuana and eleven had taken amphetamine. In contrast, most of the non-LSD patients had not used these other drugs; two of them who had, reported an occupational record like that of the patients who had taken LSD. The LSD patients had come into hospital because of depersonalization, perceptual distortion and confusion; in some cases their illness had paranoid and catatonic features. On scrutinizing the group as a whole, it would seem that only three of the twenty patients in the LSD group had psychoses which could be directly related to the ingestion of LSD.

Addiction

Social factors

Most of the available information comes from the United States. Users of the drug belong to different social strata; reports consequently vary according to which sort of LSD user has been investigated. The professional people whom Richard Blum studied are very different from the derelicts whom Ludwig and Levine questioned at Lexington. Some generalizations, however, appear justified. The tendency to recruit proselytes is strong and the atmosphere and setting in which people take the drug is as sociable as with alcohol. People who do not join in a "psychedelic session" are made to feel unsociable, timid and stuffily conventional. The drug is neither difficult to obtain nor expensive, but it could easily be contaminated with other substances since the people who write on the subject do not appear to know where the drug is manufactured illicitly or by what process. There is no evidence to suggest that crime is fostered by LSD-taking at present, but it is unquestionably associated with idleness, failure and fecklessness. There is a fair amount of information bearing on the way that social factors operative before and during intoxication influence the reaction of various subjects to LSD, but the main contributors to this aspect of the LSD problem (for example, Hyde in Boston), insist that much further study is required to determine how social and personality factors reinforce each other. Similarly, the WHO Expert Committee on Drugs, in their 1967 report, discuss sociological implications and want research done on many other aspects, such as incidence,

prevention, effect of enactments, creation of deviant groups, as well as on fairly obvious social factors which they enumerate.

Progression and combination in addicts

The evidence on "escalation" or "cascading", i.e. passing from LSD to opiates (chiefly morphine, heroin and cocaine), is scrappy and discrepant. In a group of twenty psychiatric in-patients who had taken LSD at some time, according to their own statements all but two had taken some other drug, mostly amphetamine or marihuana, but probably not heroin. Similarly, Richard Blum says that "either as a consequence of planned administration of other drugs by LSD institutions, or of informal use, the majority of persons accepting LSD had also taken other drugs by the time of this study. The use of LSD is also associated with the regular use of mind-altering drugs; whereas only 6 per cent of the controls were regular users, one-third of the LSD accepting sample used such drugs with some regularity". In another group of seventy patients, seen in a Los Angeles hospital, eight had used amphetamine during the six weeks or more before they had attended the Clinic, twenty-five had used marihuana, and four had used heroin and barbiturates. The twenty-seven narcotic addicts who were questioned at the Lexington Centre had, of course, been selected for this very attribute; some said that heroin and LSD did not mix and that the combination made them feel sick, others said they used heroin to "level off" the experience with LSD, enable them to go to sleep and recover contact with reality.

Whereas heroin is usually taken in solitude, LSD is shared and the drug is dispensed at parties just as alcohol might be. LSD is not purveyed by the methods of the venal "heroin pushers". In another recent survey, the director of a narcotics project in Chicago states that there is a tendency for people to keep to one drug; "the highest cross-over is between the marihuana and the psychedelic users"; when there are "bad trips" or difficulty in getting LSD, other drugs may be tried but on "campuses there is a very healthy respect for opiates, and distance is kept from them". (Evidently a high proportion of the subjects were or had been university students.) "They are highly gregarious in the marihuana-psychedelic circle, and, as evidence of their intellectual accomplishments and mystical leanings, they tend to have literary gods and cultural leanings. They seldom take alcohol as well as LSD."

Legislative Control

Although opinions are expressed in the psychiatric journals about the desirability, harmfulness or injustice of legislation designed to control LSD, scarcely any facts are available to test the correctness of the views thus put forward. There are some statistics about the effects of legislation intended to restrict the non-medical use of narcotics, and there are some rather vague data about marihuana, but the nearest approach to anything factual in respect of LSD is in a paper from California (Ungerleider, Fisher and Fuller) where it is stated that when the new Federal Abuse Control Amendment (making it illegal to possess LSD) came into force in February 1966 there was no diminution in the number of new patients seeking psychiatric help for undesired LSD complications; the largest number of such patients seen in any one month was seen after the coming into force of this law.

There is, however, a consensus amongst almost all who write on the subject in medical or psychological journals that unrestricted access to LSD is objectionable because, even in skilled medical hands, there have been untoward results and such effects are much more frequent and alarming in those who take it illicitly and without medical supervision. Dr. Leary and his associates, of course, do not subscribe to this view, though it is emphatically asserted by all medical writers on the subject. The issue, therefore, would seem to be not whether there should be control but what kind and degree of control or prevention, i.e. over and above limiting supply to research workers and physicians or, more narrowly, to psychiatrists and other specially qualified doctors. Several writers put forward the view that "if the drug is defined as immoral or criminal we can expect guilt, aggression and further social delinquency to result". The Chief of the Section on Psychopharmacology at the National Institute of Mental Health in Washington (Stephan Szara), in a recent address to the American Psychiatric Association, declared dogmatically "if the drug is taken by a borderline psychotic person or by a subject with personality defects in a medically unsupervised or socially unsanctioned setting, the results can be read in the criminal columns of the newspapers and in the nationwide magazines".

CANNABIS

Acute Intoxication

Physical effects

The physical effects of cannabis intoxication are raised pulse rate and blood pressure, dilated sluggish pupils, injected conjunctival vessels, tremor of tongue and mouth, cold extremities, rapid shallow breathing, ataxia and active deep reflexes. The severity of the symptoms depends not only on the dose and preparation but on the individual. A young Englishwoman on one occasion smoked two-thirds of a home-made hashish cigarette which had not upset her husband; she promptly developed gross incoordination of the hands, astasia, rapid pulse, and dyspnoea. In soldiers who took cannabis a temporary loss of consciousness has been reported, with slow irregular pulse and low blood pressure. Others have described vertigo and vomiting, and death is said to have occurred from cardiac failure or intestinal distention after gross overeating. But severe physical disturbance is rare. A common initial effect of smoking the drug is intense cough or a burning feeling in the throat and chest.

Psychological effects

The psychological effects of acute intoxication were first described in detail by Moreau de Tours:— euphoria, excitement, disturbed associations, changes in the appreciation of time and space, raised auditory sensitivity with elaboration of simple phrases or tunes, fixed ideas, emotional upheaval, and illusions and hallucinations.

Suggestibility is much increased (the assassination of General Kleber is supposed to have been carried out by a fanatic whose heightened suggestibility under cannabis made him a pliant catspaw).

In spite of widespread popular belief, there are no aphrodisiac effects. Erotic fantasies may be well to the fore, but they do not lead to action.

There is much individual variation in the psychological effects. Perhaps because of ethnic and social differences, and the effects of different preparations of the drug, widely divergent accounts are to be found in published papers. Lord Todd put it succinctly: "To give an accurate picture of the effects of hashish is extremely difficult, partly because they are more subjective than objective and because individual variation in response is probable greater with this than with any other drug. . . . Among the commonest recorded effects are a feeling of well-being alternating with depression, distortion of time and space, and double consciousness. Objectively there is a period of excitation and exaltation, followed often by sleep or coma."

Some subjects feel acute anxiety as soon as the drug takes effect; others are pleased, amused or elated, although they may be aware that their thought processes are somewhat disordered, their memory impaired and their self-control diminished. The phases of abnormality may come in waves, heralded by sudden violent headaches. The emotional state is not in keeping with the subject's situation, and, as the intoxication grows less, subjects mostly feel apathetic and depressed. During the acute stage of intoxication, they may have become suspicious and afraid that they will be permanently insane, or that their friends are

trying to find grounds for shutting them up in a mental hospital. Characteristic visual phenomena are almost invariably reported; they are not true hallucinations but illusionary falsification, greatly elaborated by some subjects. Perception of one's own body is commonly interfered with, and outright depersonalization may occur. With small doses of cannabis the effect may be wholly subjective, mild and gratifying.

The first signs of intoxication, appearing about three hours after consuming the drug by mouth, may be nausea or vomiting, with gross movements and loquacity. Disorders of thinking may be overt, or only detectable by close examination. Intoxicated persons may be unable to retain more than a single sentence, so that conversation is disjointed and may be unintelligible; a communication that has been heard and understood may be lost in a few seconds; in the middle of a lively conversation, speech may stop abruptly and the intended remark is gone beyond recovery. The disturbance of memory may be severe in one person and negligible in another. The time schedule varies according to the mode of consumption. After smoking hashish resin, acute anxiety and restlessness may come on within about half an hour, then calm and pleasant sensations supervene with visual imagery. In one to two hours the subject becomes sleepy and when he wakes from the ensuing sleep he may be able to recall details of the intoxication. If, however, he has taken the cannabis in powder form, it may take three to six hours for sleepiness to come on.

In Europeans, though the order of events may vary a great deal, a typical sequence is euphoria with restlessness, then confusion, disturbed visual and auditory perception, then a dreamy state and, finally, depression and sleep. On waking after this sleep, there may be numbness, dysarthria and some amnesia. Many Moroccans when under the influence of the drug become gay or relaxed, though it is not rare for anger to be expressed in some act of violence. According to one observer they value cannabis because it frees them temporarily from moral and cultural restraints on conduct. In contrast to the torpor described in some subjects, Moroccans may feel that they can do difficult things easily, and they may jump and dance. Hesnard, a psychiatrist who has observed Turkish and Syrian hemp addicts, described them as incoherent in speech but self-observant, talkative, exuberant, gesticulating and running hither and thither, incapable of mental work and agitated. Noisy laughter may be incongruously accompanied by sadness. Intense depersonalization sometimes occurs. They have erotic desires which they do not translate into erotic behaviour. In Brazil, according to Wolff and other Brazilian psychiatrists, the picture is different from that described elsewhere; sexual orgies are alleged to take place.

The discrepancies in published accounts of acute intoxication may be in part accounted for by individual constitution and the effect of adulterants, also by differences in dosage. Practised hashish consumers have usually learned how to regulate the dose of whatever preparation they use so that the disagreeable effects are minimal.

Psychotic features

Among the symptoms of *acute* intoxication gross mental disturbances are described which can properly be called psychotic. They are usually the outcome of taking a fairly large dose of the drug; and the clinical picture is that of a severe

exogenous psychosis—delirium with confusion, disorientation, terror or anger, and subsequent amnesia about what happened during the period of intoxication. Although most often described in countries where cannabis is widely resorted to, striking instances are reported also in Europeans.

Within this acute setting, the most frequent psychotic features are paranoid delusions of being pursued or controlled, delusions of preternatural abilities, strong inclinations to suicide which are not carried into action unless associated with panic, and irritability. Waxy flexibility and other catatonic features have been observed, though infrequently.

The impulse to suicide may be very strong; a doctor who took forty drops of tincture of cannabis indica developed at first great anxiety and fear of death, then "I was possessed with an almost irresistible desire to commit suicide by rushing to the adjoining canal or cutting my throat with the knives on the table close by, though no attempt was made at doing so. Shortly upon this, I was seized with fits of alternate laughter and crying, without any apparent cause. When the symptoms were subsiding my appetite became ravenous accompanied by great thirst. . . . I experienced no pleasurable intoxication or feeling of happiness, but the very reverse."

There is a sharp contrast between the ecstatic and relaxed state described in many reports and the restless activity occasionally observed (along with exaltation, irritability, emotional excess, noisiness and even reckless violence) in some subjects, especially in the Punjab or in Brazil. Evidently, large doses produce anomalous effects, seldom seen in mentally stable persons or in those who have learned to regulate their intake so that it should be pleasurable. An example of how excess can affect the individual is provided by a French youth aged 20 who smoked five hashish cigarettes straight off. He became very agitated and restless, rushed around Paris and, eventually, fourteen hours after he had taken the drug, he went into a police station to give himself up for having murdered his stepfather (an entirely baseless delusion). The duration of the psychotic intoxication was longer in his case than is usual; as a rule, the condition clears up in three to six hours.

Psychological studies

These have suffered from the limitation that they were carried out either on highly selected subjects—prisoners and drug addicts—or on very small samples, sometimes only two or three persons. The main findings have been that simple functions like tapping speed and reaction time were very little affected by moderate doses of cannabis, but that steadiness of hand movements and complex reaction time were adversely affected, the maximum change occurring about four hours after ingestion.

In intellectual tasks speed and accuracy were impaired, the degree depending on the dose. Surprisingly, the ability to estimate short periods of time was not reduced in an American study, but the subjects were chronic addicts, whereas in an experiment carried out by two psychiatrists on each other under laboratory conditions, time intervals were overestimated. Two German psychiatrists examined thirty normal subjects, and found three types of intellectual disorder—incapacity to fuse details into a whole, reduced memory storage, and blocking; these observations were made, however, after the drug had been administered in the form of cannabinol.

Effect on persons already psychotic

In the 1930's, experiments were carried out on schizophrenic and depressed patients in mental hospitals to see what cannabis would do to them and how far the drugs, alleged to be psychotomimetic, would intensify psychotic symptoms. The findings were not uniform. Affectivity was altered but in different ways and degrees; some schizophrenics became euphoric and hyperactive, others became catatonic; surprisingly, only two-thirds of the schizophrenics developed hallucinations. Some of the depressed subjects became euphoric, others passed into a depressive stupor. Autism was intensified in some schizophrenics and symptoms that had previously cleared up were revived. The schizophrenic patients showed less change in time and space perception than normal subjects while under the influence of the drug. Impulsive acts were more prone to occur in schizophrenic subjects than in normal cannabis users.

Benefits and Therapeutic Use

Benefits have been claimed from cannabis, but trustworthy reports have been few and vague. It is said to promote relaxation and calm after the trials of daily life, and to assist shy people to enter into warm social relations; it lessens awareness of pain and misery, helps to allay neurotic anxiety, and is an aid to religious fervour. A prominent American psychiatrist recently wrote, apropos of eleven university students who had had severe adverse reactions from cannabis, "The evaluation of the harm a drug does requires some consideration of its benefits. Users of marihuana state that it is a source of positive pleasure, that it enhances creativity, that it provides insight, and that it enriches their lives. These are hardly minor claims. All but two of the eleven individuals reporting adverse reactions considered the benefits to far outweigh the unfortunate aspects and planned to continue use of the drug."

From ancient times, cannabis has been credited with therapeutic powers, especially in India. Its introduction into Europe in the mid-nineteenth century led to the familiar burst of enthusiasm for a new remedy. This dwindled as time passed but died slowly: "During the period 1840 to 1900, there were something over one hundred articles published which recommended cannabis for one disorder or another." Its vogue preceded the advent of synthetic hypnotics and analgesics, and it was lauded for its effect in alleviating pain, migraine, insomnia, dysmenorrhea, difficult parturition and cramps. In 1890, Russell Reynolds wrote that "when pure and administered carefully it is one of the most valuable medicines we possess".

It was also said to be good for mental disturbances though its proponents rather shamefacedly acknowledged that this line of treatment had a homeopathic flavour. As late as 1928, an article appeared reporting that cannabis was valuable for severe melancholia and there are still a few who assert the therapeutic value of the drug. Because it heightens suggestibility and weakens inhibitions, they find it a useful adjuvant in eliciting submerged memories and feelings which the patient cannot otherwise communicate. Its antibiotic powers have been explored in Central Europe.

Initiation: Social setting

Most of those who take cannabis in any society have been introduced to the habit by an acquaintance. The amount of pressure varies from country to country—the commoner the habit, the more ready the compliance—and from group to group. In Egypt (where penalties are severe and include capital punishment for trafficking), the habit is nevertheless very widespread, and, as was shown by a recent investigation on 253 men who had used hashish at least once a month during the previous year, conformity to the ways of the group emerges as a powerful factor, especially among those who have been led to expect a blissful experience and sexual stimulation from it. Taking it is a convivial affair; four to six friends meet in the evening, smoke and engage in light conversation. Similarly, an American report confirmed the view that marihuana is a socially utilized intoxicant, seldom taken in solitude. Those who have studied American college students who smoke marihuana conclude that they do so because they are alienated from the values of adult society which exposes them to conflicting demands; through this habit they can mortify their parents and flout authorities. This is a speculative interpretation of their motives.

The fullest available description of the social conditions which foster the marihuana habit comes from Oakland, California. It counterbalances, and perhaps corrects, the picturesque and alarming observations made on more degraded, psychopathic, criminal, or poverty-stricken and under-nourished groups. The investigators obtained the confidence of the youngsters, mostly Negroes and Mexicans, through providing them with club amenities without strings. They were firm in their conviction, based on their own experience, that the use of such drugs as marihuana results in harmless pleasure and increased conviviality, does not lead to violence or madness, can be regulated, does not lead to addiction, and is less harmful than alcohol. They were not interested in being helped to abstain from marihuana, and they cited case after case of individuals known to them who had not suffered deterioration in health, school achievement, athletics or career as a result of their habit of smoking marihuana. Boys who take the drug in excess were considered by the rest to have a weak personality.

There are several patterns of use and users among these youths. They themselves recognise four types for which they have cant names. The "rowdy dude" wants to impress and frighten others; he has difficulty in getting marihuana from other youths because he is reckless and irresponsible and they fear he will get them into trouble with the police; he is subject to pressures which direct him towards becoming a criminal or an opiate addict. When he stops taking alcohol or sniffing glue the "rowdy dude" may settle down, and start to take marihuana instead. In that case he becomes a "pot head" who limits himself to marihuana smoking, or a "mellow dude" who uses amphetamines or barbiturates or methedrine as well as marihuana. Both "pot heads" and "mellow dudes" value *sang-froid*. They believe themselves to be intelligent, daring, cool-headed, worthy of respect, and they do not resort to violence; they remain at school or at work and engage in athletics. They will smoke marihuana three or four times a day, especially if they are going to a party; they believe it breaks through their shyness in approaching girls and increases the pleasure of sexual intercourse. The fourth

type is the "player", an older youth who sells drugs and becomes a violent criminal or a pimp or fence; he may take to heroin but will mostly be on his guard against any drug that may reduce his alertness.

Initiation into marihuana-smoking in this group is usually effected through the desire to emulate older boys. The Oakland investigators reject firmly the usual assumption that those who take to the habit are mainly influenced by emotional disturbances and social stresses. Their observations do not support the explanation which regards marihuana use as an effort to escape from reality or to vent underlying hatred of organized society. They conclude that "induction into drug use is a developing experience that depends on access to drugs, acceptance by drug-using associates and the kind of image that youngsters have of drugs". So far from retreating from reality, marihuana-users are held to be making a positive effort to be in the mainstream. The investigators likewise reject the notion of a steady progression from marihuana to crime and opiate addiction. It may occur, as the four types indicate, but most users steer away from these courses. Many of the Oakland youths had experimented with heroin, but only four had become addicts.

The summary conclusion by the Oakland observers is unequivocal: "Youthful drug use in Oakland is an appreciably extensive and deeply rooted practice, lodged primarily in the lower strata, but currently expanding into middle and upper class strata. It is woven into a round of adolescent life as a collective practice . . . and is buttressed by a body of justifying beliefs and convictions, involves a repertoire of practical knowledge and incorporates a body of precautions and protections against apprehension or arrest. Drug use constitutes for the users a natural way of life and does not represent a pathological phenomena."

The age at which use of the drug began, according to practically all the studies reported, was in adolescence, though children have sometimes begun before puberty. In a group of American negro soldiers who had been admitted to hospital because of their cannabis-taking and its ill effects, 13 per cent said they had started doing so before adolescence and two-thirds before they were seventeen.

The majority of users, apart from university students, belong to the urban proletariat. In Nigeria, where the habit has only recently been developing on a large scale, the people mostly affected had drifted to the city and live on the fringe of organised society. Others who take it are long distance lorry drivers who believe that it increases staying power and courage, enabling them to take daredevil risks. Among twenty-six cannabis-using patients admitted to Aro Hospital in Abeokuta, eight were lorry or taxi drivers. In North Africa, the rural population is also affected, but much less so than the industrial workers and the unemployed who are often under-nourished. During Ramadan there is a rise in the number of cannabis-takers that have to be admitted to the mental hospital. Among cannabis users from Upper Egypt, who are predominantly rural, there is a larger proportion of people with average or above average incomes than in those from Cairo. In several Asiatic countries the well-to-do smoke or otherwise consume their cannabis in private and in moderation; they do not get into the statistics or serve to tone down the published description of the coarse effects of cannabis.

In Morocco, Nigeria and some other African countries taking cannabis is not exclusively a masculine preserve, though women who do so are far fewer than men. In South Africa, 10,044 male Africans and 632 females were convicted of

possessing cannabis; for Europeans, the corresponding figures were respectively 181 male and 4 female.

There is no convincing evidence that, other things being equal, the nationals of any particular country are more prone to take cannabis than, say, Englishmen or Burmese. In American reports, especially those based on military experience, Negroes and Puerto Ricans are to the fore, but this is adequately accounted for in terms of the psychological, economic and civic background of their lives.

It is impossible at present to disentangle the psychological, climatic, social and religious factors which may determine the range and style of cannabis-taking. Confident statements about one or other such influence rest on impressions and conjecture. There are sweeping generalizations (such as that Moslems use cannabis because they are forbidden alcohol, whereas Hindus prefer opium) and detailed accounts of the extraordinarily diverse ways in which the drug is prepared and taken in different countries. Ethnic factors are loosely invoked, but never with adequate evidence. It has been asserted, for example by a psychiatrist who had had extensive experience in Algeria, that hashish is suited to the dreamy and contemplative temperament of the Moslem and alcohol to the hyperactive Westerner. Another authority, well acquainted with the Moroccan situation, says that the people of that country are imaginative and emotional, and that they gain relief through the drug when they are in distress. A German psychiatrist, who had spent two years in Morocco, reported this year that impulsive behaviour under hashish can be attributed to "the Moroccan mentality", which is also "prone to trance states". Another, with long Egyptian experience, attributes the growth of the practice there to foreign domination, the prohibition of alcohol, and the special tribunals for foreigners which made illicit traffic easy and safe. A Brazilian doctor maintains that dwellers in the lowlands need cannabis, while those who live and work in the high plateaux of the Andes need the coca leaf to sustain them amid the extreme rigours of their lives.

Apart from the Brazilians and adherents of the Ras Tafari cult in Jamaica, a direct association with contemporary religions has not been reported; the continuing role of cannabis in Ayurvedic and Unani medicine cannot be regarded as being of a religious nature.

General attitudes

The attitude of the general public towards cannabis is not constant, nor evenly spread through the different sections of society. According to most observers in India, and particularly in Bengal, taking the drug is not regarded with disapproval. Sixty or seventy years ago, however, most of the population looked down on the drug-takers, largely because of the degraded class they came from; but consumption of the drug by sadhus, who were in many cases deeply committed to the habit, was viewed tolerantly. The public attitude in Mexico has also been reported to be tolerant. Satisfactory information about the attitude of various sections of Western society does not exist; inference from newspapers tends to be inconsistent.

Personality

Whether, or how far, particular features of personality conduce to the establishment of the cannabis habit is a highly contentious question, as much so as in

the case of alcohol. At one extreme are those (like P. O. Wolff reporting on the peasants of Brazil) who deny that there is any predisposition, and at the other those who regard defects of personality as prepotent—not only in bringing about habituation, but also in determining the form of psychological disturbance produced. Since the estimates of personality are made in almost all cases retrospectively on persons known to be cannabis-users, there is much uncertainty as to whether the traits described were consequences of the habit or had preceded it and favoured its development. The temperamental qualities most often cited as predisposing are anxiety, impulsiveness, shyness combined with a longing for social contacts, immaturity, emotional instability and various neurotic and psychopathic features. They are clearly unspecific.

Two American psychiatrists who studied a hospital group of cannabis-takers concluded that "the personality pattern of these men is one of strong libidinous desires resulting from early home conflict, a weak ego which identifies with an undesirable farther image, and a super ego created by the moral mother. . . . Use of marihuana removes the super ego which, in turn, strengthens the ego and enables it to satisfy the libidinous desires at various levels of infantile behaviour". Another writer, less psychoanalytically recondite, has found that homosexual tendencies are at work among the men who take cannabis to excess. A respectable body of opinion is to the effect that, though there is no doubt that faults of character may be found in those chronic users who reach hospital or prison, the majority of moderate users are within the normal range of personality. This is in sharp contrast to reports like that on the United States marihuana-smoking soldiers in the Panama Canal Zone which found that 85 per cent of the men were mentally abnormal, 62 per cent were classified as constitutional psychopaths and 23 per cent as morons.

Prevalence

There are notoriously great differences between countries in the prevalence of cannabis use, but reliable estimates do not exist. Surmises are based on the quantities of the drug seized by the police, the number of convictions, and the proportion of people in mental hospitals who admit to having taken it. The figures thus arrived at are very high for some countries. Thus the most recent assessment for Egypt is that 27,000 kilograms of hashish were smuggled into the country to be used by about 80,000 habitués (out of a total young male population of some three million persons). Gross figures are calculated for Morocco (50 per cent of the population—"a million habitués"), and for some other countries. It is difficult to regard these as more than guesses.

The same uncertainty holds good of current estimates in North America and in Europe. A recent cautious statement, based on United Kingdom convictions for possessing or using cannabis, arrived at a figure of 30 regular users per 100,000 of population, and as many more who have tried it a few times.

Interest has centred on university students. In a sample of London students, 4 per cent have been said to be steady users and 10 per cent occasional users, but, because of penalties, fluctuations of opinion and other obstacles in the way of a trustworthy survey, such a finding cannot be generalised. It has been reasonably stated that the amount of addiction to a drug in any given population is a composite of availability, price, legal codes, suggestion, cultural attitudes, psycho-

logical needs and socio-economic factors; the product of such mixed influences could hardly be unchanging. In a questionnaire, to which 1,245 students replied at Brooklyn College, New York, it emerged that progression to other drugs very seldom occurred, though three-quarters of the students had, at one time or another, experimented with marihuana. One-third had done so on only one occasion.

Adverse Effects of Abuse

Social effects apart from crime and psychoses

Observers with long experience concur in the opinion that continued excessive use of cannabis over a period of years leads to moral and social decay; countries from which such reports come are South Africa, Morocco, Algeria, Tunisia, Syria, Turkey, Astrakhan and India. In a few reports, such conclusions are extended to cover chronic use of the drug in only moderate doses, but the majority of observers distinguish between heavy dosage and restrained use. Restrained use is widely regarded as harmless in its effects, provided the consumer had, from the outset, a healthy mental constitution. In defining healthy mental constitution, circular reasoning is apt to creep in.

The Mayor of New York's Committee on Marihuana found that people who had been smoking marihuana daily for years showed no abnormal psychological functioning which would differentiate them from non-users, but the population selected for study was composed mainly of men in prison who had volunteered; they were hardly a representative sample of users and non-users. The Indian Hemp Commission of 1894 reported, after an elaborate enquiry, that moderate use produces no injurious effects except in persons with neurotic diathesis, but that excessive use may intensify mental instability and moral weakness, and lead to loss of self respect.

The degradation that most writers report in the excessive chronic cannabis-user is apparent in several ways. He is irritable and impulsive, or inert and dreamy; he neglects himself grossly and is incapable of sustained effort; he may become a beggar or a vagrant, taking no responsibility for his family; he may practise homosexual or other sexual abnormalities or become impotent; he may be hypochondriacal or apathetic. His unkempt and prematurely aged appearance, inflamed eyes, tremor, and malnutrition are said to make up a fairly characteristic picture.

Effect on occupational capacity

Because of his impaired judgment, especially of space relations, and his irresponsibility, the chronic user—as well as the person acutely intoxicated—is dangerous when driving a car or lorry; this has been reported particularly from African countries. But the general occupational record of chronic users is not invariably bad, and no one has succeeded in determining how many continuous users become incapable of regular work. Bouquet and others have pointed out that there are some men who have been smoking hemp for thirty or more years and continue to follow their occupations satisfactorily: "A few daily pipes of kif are merely an agreeable weakness, enough to produce the condition of well-being they desire. They rest content with that." In contrast, a pronouncement in the

United Nations Commission on Narcotic Drugs stated that "the study points up unequivocally the danger of cannabis from every point of view, whether physical, mental, social or criminological".

Crime

Published statements regarding the association between crime and cannabis illustrate the confused and contradictory standpoint taken up by experts, and the loose reasoning evident when a causal nexus is being considered.

Taking the views first of those who believe that cannabis can bring about criminal behaviour, some uncompromising conclusions are put forward, e.g. "literature surveys and personal contacts have clearly demonstrated the association between the use of marihuana and the commission of various crimes". Several describe outbursts by chronic users in which they are wildly agitated and, seizing some handy weapon, attack a nearby person, often without the faintest motive for hostility: "murders are frequent and motiveless". A Greek investigator inquired into the subsequent history of 170 people who were arrested between 1919 and 1950 for possessing cannabis but had not previously been before a court for any offence; he found that 117 of these were subsequently sentenced for crimes of violence, blackmail and similar serious offences. P. O. Wolff wrote in 1949 that the drug had given rise to "a most appalling percentage of the tragedies and crimes in Cuban society", and described similar consequences in Brazil. One of the outstanding French authorities on cannabis recounts the sequence of events he has often observed in victims of chronic intoxication. They pass into a state of torpor in some secluded spot, then abruptly they become agitated and the slightest opposition moves them to violence, or perhaps to sexual crimes (especially if they combine other drugs with their cannabis). A Moroccan investigator also emphasizes the lack of adequate motive or premeditation in the outburst of persistent, often murderous, violence. Arson is fairly common. In several respects the impulsive attacks may be like those of an epileptic, occurring in a state of disturbed consciousness. Lesser crimes, such as theft and procuring, are common, but do not seem to have evoked in observers the strong feeling, indicated by such epithets as "heinous", "savage", which are applied to the outbursts of violence. Running amuck is considered by some to be a manifestation of chronic cannabism.

Opposite these supporters of the view that cannabis causes crime are the almost equally numerous and authoritative writers who deny any direct causal connection, though they do not dispute the frequent concomitance of cannabis and crime. The most influential and, in some respects, the most thorough enquiries, were made by the Indian Hemp Commission of 1894 and the Mayor of New York's Committee in 1944. The former concluded that "the connection between hemp drugs and ordinary crime is very slight indeed", but that excessive use does, in some very rare cases, make the consumer violent; six hundred witnesses were asked by the Commission whether they knew of cases of homicidal frenzy, and very few had. A considerable majority of the witnesses did not consider that the drugs produced unpremeditated crimes of violence and some said (as other writers have since) that there is a negative relation because as a rule cannabis makes men quiet. The Mayor's Committee reported to a similar effect; many criminals might use the drug, but it was not the determining factor in the commission of major crimes.

Eight observers in Brazil reported in 1962 that an exhaustive inquiry which they had made in the jails and hospitals had not produced any evidence that cannabis is an important cause of crime. This finding runs sharply counter to Wolff's observations in the same country.

Similar negative conclusions about the causation of crime in cannabis-takers come from Vancouver, the American Armed Forces abroad, New York, California and Nigeria. The Nigerian psychiatrist (Asuni), who examined a series of cannabis-takers, found no major crime among them except in one man who was schizophrenic, and another imprisoned for reckless driving. His general findings are in keeping with the moderate contemporary view, viz. that there is an antecedent predisposition towards psychopathic or criminal behaviour in those cannabis-users who do commit crimes, the cannabis often merely revealing or intensifying abnormal tendencies; and that circumstances arising from cannabis-taking may have fomented criminal conduct; "The people involved in cannabis-smoking . . . tend to be driven underground. In this situation their sense of isolation from the main body of society gets intensified. Their sense of value also changes to that of their new subculture, and this new sense of values may be generally asocial or anti-social". The Medical Director of the Lexington Narcotic Center in 1947 described the same downward progression: "It would be difficult for a normal personality to undergo such experiences without harm; for the type of personality that seems to be the background for addiction, they may cause irreversible distortions." Unfortunately, the type of personality that predisposes to cannabis-taking has not so far been described or identified convincingly.

Probable reasons why there should be flat contradiction between the findings of different observers are (1) that criminals in some countries base their defence on alleged cannabis intoxication which provoked behaviour that they cannot remember and for which they cannot be held fully responsible (just as epilepsy is often entered as the defence in our courts for crimes of violence); (2) that many who use cannabis in various countries combine it with opium, heroin, amphetamine, barbiturate or alcohol, and it is impossible to tell which, if any, of these is to blame for the criminal behaviour observed in a given individual; (3) the samples of persons investigated have mostly been small and the history of drug-taking, its duration and degree in each individual has been provided by the man himself, who often believes it to be to his interest to lie about it.

When criminal behaviour occurs in people who take cannabis steadily, it is by some confidently assumed, and by others confidently denied, that the crime was caused by the cannabis, though the available data are insufficient to permit a judgment either way. Only rarely in published reports on criminals and cannabis has a satisfactory effort been made to distinguish between chronic cannabis-use and infrequent or casual experimentation, or between criminals who have recognizable mental disorders and those who are mentally normal, apart from the criminal episode.

The one delinquency which receives general reprobation is driving while under the influence of cannabis whether on an isolated occasion or when bemused by chronic excess.

The old story that cannabis was taken to nerve men to go into battle and to commit murders to order, has little or no foundation except perhaps that the mercenaries employed to put down riots and revolts in India were, according to

the Indian Hemp Commission, habitual consumers of cannabis who acquired "Dutch courage" thereby. As mentioned earlier, advantage may be taken of the heightened suggestibility of the cannabis-user.

The most likely relation that emerges from the welter of conflicting statements is that chronic or excessive indulgence in cannabis may, in some people—a small minority of the male public at risk—lead to attacks of disturbed consciousness, excitement, agitation, or panic, and reduce self control. The extent to which the affected person may commit a crime in this state of mind depends more on his personality than on the dose or preparation of cannabis which he has been taking.

Psychoses

"Cannabis psychoses" have been frequently described and the accounts include practically every known variety of mental disorder. The predominant and most frequently put forward are schizophrenia—especially catatonia, paranoid states, manic excitement, depression, anxiety, and dementia. A writer on the subject whose report (1903) has been often quoted or borrowed, was Warnock, the Medical Superintendent of the mental hospital in Cairo. He had recognized as hashish psychoses an acute hallucinosis with restlessness, incoherence, and a manic condition; but he added that "besides these types, there are numbers of cases of chronic mania, mania of persecution and chronic dementia, alleged to be produced by hasheesh, but I have no means of verifying these allegations". He also wrote: "I doubt very much if hasheesh insanity can be at present diagnosed by its clinical characters alone." This is a cautious view; other observers who have seen many patients to whom they gave this diagnosis dwell on dementia as a fairly common outcome of chronic use of the drug, or assert that there is a typical and striking uniformity of symptoms in the cannabis psychosis. An Indian psychiatrist, Dhunjibhoy, defines it: "A patient admitted to an Indian mental hospital with intense excitement, grandiose ideas, tendency to wilful violence, a peculiar eye condition (marked conjunctival congestion), total amnesia of all events, attacks of short duration, followed by complete recovery, with a history of the drug habit and without a psychopathic or neuropathic heredity, is a typical case of hemp insanity". Some observers describe severe mental deterioration as a familiar outcome, while others with much experience say this does not occur at all.

The term "cannabis psychosis" begs the question of the existence of such a syndrome. On the one hand, there is a crowd of witnesses qualified to speak by lifelong contact with the problem in mental hospitals of countries in which cannabism is very common and they are convinced that the condition is correctly identified. "The effects of the drug are detailed in all the well-known text-books and that its abuse is a direct source of serious mental disorder is indisputable", wrote a senior doctor of the I.M.S. in 1923. A high proportion of the patients admitted to mental hospitals in India and Egypt and elsewhere were diagnosed as falling in this category. On the other hand, there were equally informed doubts as to the legitimacy of the diagnosis in many cases. These doubts were cogently expressed by the Indian Hemp Commission in 1894. Out of 1,344 admissions to the asylums of India during 1892, there were only 98 patients in whom the use of hemp drugs could reasonably be regarded as a factor in causing the insanity, and in 37 of these there was a clear history of some other cause which might have

co-operated with the hemp drugs. The Commissioners concluded, after an enquiry of still unequalled scope, that "the usual mode of differentiating between hemp drug insanity and ordinary mania was in the highest degree uncertain and therefore fallacious. . . . The excessive use of hemp drugs may, especially in cases where there is any weakness or hereditary predisposition, induce insanity. It has been shown that the effect of hemp drugs in this respect has hitherto been greatly exaggerated, but that they do sometimes produce insanity seems beyond question." Nevertheless, it has been questioned. Even so guarded a statement implies that there are some sure criteria for establishing the causal role of the cannabis, either when it has been established that a man exhibiting a so-called "functional psychosis" had previously been for years smoking or eating cannabis, or when such a history precedes the onset of an "exogenous psychosis" exhibiting the cognitive and other defects attributable to physical or chemical damage to the brain. As a rule the writers on the subject do not give enough detail to warrant any attempt at retrospective diagnosis, but, in those who do, there are instances of persistent confusional syndromes shading off with the passage of time into chronic dementia in which the cannabis seems to have been the major cause.

The reasons for the discrepancy in opinion expressed by equally experienced observers seem to be:—

(1) The notion of a single cause for mental disorder, widely held in the last century, is no longer regarded as tenable. Consequently, the last two decades have seen few assertions about cannabis being *the* cause of insanity, but many espousing the view that it has been either a necessary or a contributory cause, especially where evidence of predisposition to psychosis is forthcoming from a patient's previous personality and health record.

(2) The clinical picture of what has been regarded as cannabis psychosis has not had any characteristic features (such as delirium tremens has, for example). It has often been indistinguishable from schizophrenia.

(3) The reasons put forward earlier for the discrepant opinion about crime and hashish apply here.

4) In many of the published reports it is made clear that the hashish was combined with other substances—datura, alcohol, heroin or amphetamine —which could be responsible for the psychosis which developed. The cannabis might have had nothing to do with it.

(5) The history of the patient's previous mental state has been only cursorily enquired into, often for lack of dependable informants. Many of these patients may have had established or incipient mental illness, quite independently of cannabis, before the incident—a crime or a catastrophe—which brought them into a mental hospital.

(6) The diagnostic methods employed in many studies were, by any reasonable standard, woefully inadequate. In one large area, the diagnosis might be made by a policeman. The long-standing belief that cannabis causes insanity could strengthen this diagnosis in a doubtful case. Ingrained beliefs and habits are known to be powerful enemies of unbiased diagnosis.

There is no unequivocal evidence that cannabis can be the major or sufficient cause of any form of psychosis. Neither is there clear evidence that moderate euphoriant or tranquillizing doses, even if taken over a long period, do mental harm in the majority of people of average mental stability, though rare isolated cases are on record in which persons apparently in good mental health have reacted with a pronounced mental disturbance to moderate doses. In large doses, cannabis can result in severe psychosis which may not clear up; it can be of the schizophrenic paranoid form with anxiety or excitement. It is usually assumed that persons constitutionally predisposed to psychosis will be those most vulnerable to cannabis; but although this is in keeping with current psychiatric theory, it lacks experimental or statistical confirmation. In many cases it could be argued that the patient would have fallen ill with schizophrenia or other psychosis even if he had not had any cannabis. This would be a weak contention if it were not so often stated by clinicians that the "hashish psychosis" may be indistinguishable from schizophrenia.

Tolerance and Physiological Dependence

Even on such straight-forward matters as tolerance and the development of physiological dependence, there are contradictory statements. Practically all informed opinion is satisfied that neither of these develops; yet there are statements to the contrary. "Quite serious disorders are observed in those addicted to the drug over a long period when their poison is removed. Attacks of physical prostration and intellectual apathy, especially, are noted" (Bouquet). A Turkish and an Egyptian observer separately describe how the patients increase the quantity of cannabis they take in order to maximise the pleasurable effects. In Russia, Skliar has observed severe symptoms after withdrawal of "anascha"; among them were anxiety, pains in the limbs, vomiting, diarrhoea, sweating, yawning and depression, all of which would clear up quickly if some of the drug was administered. (There seems, however, doubt as to whether opium and cocaine may have been mixed with the cannabis in "anascha".) Frazer in 1949 observed states of extreme violence and confusion developing in Indian soldiers whose supply of cannabis had been abruptly stopped. To round off the picture with a paradox, Meunier and Richet found that the human organism becomes more sensitive to hashish the more it is taken, with the result that the dose could be gradually lessened to half without diminishing the effects.

Although it is said that many of those who take to cannabis prefer it because they know they can stop it without any disagreeable withdrawal symptoms, several observers agree that the psychological symptoms which develop on withdrawal can be very disagreeable, the main ones being loss of appetite, dyspepsia, pain in the abdomen, fatigue, insomnia, agitation, palpitations and headache.

Combination and Progression

In some countries, notably India and North Africa, it was not uncommon for cannabis to be combined with datura, opium, alcohol or heroin. Immigrants into Israel from North Africa, the Near East or the Middle East were "prone to take any narcotic drug they could lay their hands on".

Progression from cannabis to heroin, morphia or cocaine is the subject of

discordant conclusions, often based on concordant data. From many countries, including the United States, come reports that a very high proportion of all heroin addicts have previously taken cannabis, and that once they have progressed to this stage they seldom return to it. What determines the progression is contested. The majority of observers attribute it to association with friends or acquaintances who have themselves become heroin or cocaine addicts; others suppose that it arises from dissatisfaction with the relief or pleasure to be obtained from cannabis, and a minority postulate a predisposition to marihuana which is also a predisposition to heroin. No one suggests that there is a truly pharmacological reason why such "escalation" should occur. Some hold that in a large proportion of cannabis-users, especially adolescents, there is some obscure but powerful factor (which could be psychological or social) greatly increasing the risk that they will take to opiates sooner or later; other authorities maintain that the transition from the marihuana stage to the heroin stage occurs only in a small minority of marihuana-users and that there is no more justification for indicting marihuana as a preliminary to dependence on narcotics than for indicting coffee or tobacco.

Into this darkness some light is cast by a recent study of 2,213 addicts admitted to Lexington and Fort Worth hospitals during 1965. The patients were classified according to the state they came from, the opiate they had been taking and whether they had been marihuana-users or not. In each of sixteen states, more than 50 per cent of the subjects had used marihuana as well as opiates. In each of twelve other states, most of the opiate addicts had never used marihuana. The dominant sequence of events had been marihuana-smoking, arrest, and then opiate use; the respective mean ages in years for these three events were, first marihuana-use at 17, arrest at 19, and then onset of heroin use at 20. When the marihuana-users were compared with the non-users of this drug it was found that the former were twice as likely to be heroin addicts and to secure their drugs from underworld pushers as the addicts who said they had never used marihuana. They also had an earlier age of arrest and of onset of opiate use. Ball and his colleagues who made this study conclude: "As to the issue of association, marihuana-smoking is seen as a predisposing influence in the aetiology of opiate addiction in the United States. Among metropolitan residents of the high addiction Eastern and Western states, opiate use is commonly preceded by the smoking of marihuana cigarettes and arrest. Thus, both marihuana-use and delinquency are predisposing factors within the metropilitan host environment. . . . Enough is now known about the association of marihuana and opiate use to delineate the dominant relationship of these two events. The incipient addict is predisposed to opiate addiction by his use of marihuana for the following reasons: marihuana is taken for its euphoric effects, it produces a 'high'; both marihuana and heroin are only available from underworld sources of supply; both are initially taken within a peer group recreational setting; both are illegal: the neighbourhood friends with whom marihuana-use begins are often the same friends who initiate the incipient addict to the use of opiates. . . . Data of the present study support the conclusion that marihuana-use is closely associated with opiate addiction in the high drug use metropolitan areas of the East and West, but not associated with opiate addiction in twelve Southern states."

This detailed and temperate study lends support to the view that marihuana-users are more likely than non-users to progress to opiate addiction.

In many countries laws have been passed which make possession and use of cannabis an offence; in some, the penalties are very severe, and may include capital punishment for trafficking in the drug. The extent to which the laws are enforced varies greatly. Penalties and sentences are often equated with those considered appropriate for heroin and morphine addicts: the Medical Director of the Federal Bureau of Prisons in Washington, D.C. said in 1962: "In our Federal prisons we have about 160 marihuana offenders; the average sentence of the group is nearly six years, which is approximately what the average sentence for (all) drug offenders is."

There are diverse opinions about the effectiveness of penal legislation. A few believe that it has a deterrent effect; thus a Greek observer is sure that the power of advertising is so great that if the sale of hashish were legal in his country, very large numbers of people would take to the drug. Others review the fluctuations of state policy in their own country, veering from rigorous application of severe laws to lax administration and tolerance, and conclude that the laws have not achieved their purpose. Reading the contrasting statements on this matter it seems that most persons with relevant experience would like to have legislation applicable to the excessive user and the trafficker, but that they object to blanket legislation which permits, and even encourages, the imposition of long terms of imprisonment or other stringent punitive measures. It is generally acknowledged that it is not so much the law as the way it is acted on by the police, customs officers and magistrates that determines its efficacy (which, in any case, is limited). Lindesmith, advocating that legislation should be on the same lines as for alcoholism, gives as an example that persons driving a car while under the influence of marihuana might be fined and deprived of their licences for a period of time: "Laws such as this, with penalties of a reasonable nature, would probably be more effective than those now in effect because they would be more enforceable and more in accord with the nature of the problem being dealt with. They would have the effect of reducing the discrepancy that now exists between the laws as written and the laws as they are actually enforced."

Total prohibition of all indulgence in cannabis was firmly rejected by the Indian Hemp Commission in 1894: "The Commission now unhesitatingly give their verdict against such a violent measure as total prohibition in respect of any of the hemp drugs." Their chief reasons were that cannabis is, in moderation, harmless, that its withdrawal would excite much resentment among the population, especially the poorest sections, and that, if it were forbidden, the people would take to more dangerous drugs. But they went on to say: "While opposed to this amount of interference, the Commission feels strongly that a regulating influence is necessary and should, in future, be exercised by the Government of India over the various systems of administration of the excise on hemp drugs."

The fear that the prohibition of hashish would result in recourse to worse drugs such as heroin, datura or alcohol, has been expressed by several workers, especially those with Tunisian experience. An outstanding authority (Bouquet) wrote in 1951 that if cannabis had been absolutely prohibited thirty or thirty-five years ago in North Africa, the problem would now be manageable but the point has been reached at which suppression would result in an increase in heroin addiction. There is, however, some inconsistency in this matter. Writers who fear

that total prohibition would lead to worse dependence on other drugs, at the same time advocate determined police action to cut off all clandestine supplies of cannabis—a measure which, if successful, would surely have the same effect as total prohibition. A variant of this fear is voiced by the W.H.O. Expert Committee on Mental Health (1967) who say that "condemnation by society may arouse guilt feelings in the user, drive him to even greater dependence on drugs, and prevent him from seeking treatment".

Another observer, chiefly concerned with comparing United States with English methods of dealing with narcotic addiction, emphasised in 1962 that in America people were driven by social, legal and economic pressures to band together to establish their own group way of life, or subculture: "Addiction as such may not be as antisocial as the kinds of behaviour forced on the addict by the punitive approach to addiction." The more cannabis-taking is driven underground, or the more it is punished by imprisonment, the greater, according to some writers, is the likelihood of cannabis-smokers being corrupted and turned permanently towards antisocial behaviour of other kinds.

Partial prohibition or indirect measures of control have been tried in many countries. The commonest methods are by taxation and setting up a government monopoly. Neither, from the statements of those who have had experience of the effects, has proved effective in limiting the spread or reducing the prevalence of the habit. A few observers have urged that the risks can be reduced by suppressing the resin or other concentrated form while tolerating the powder; or by harrying and supervising adolescent marihuana-users, on the assumption that if they could consume as much as they wished whenever they wished there would be a much larger number of serious chronic victims—"wretched ragamuffins who are a danger and a burden to society." But these assumptions and assurances are made on the strength of the particular writer's experience; they lack statistical or other firm support.

It is generally agreed that taxing the drug does not deter the inquisitive or venturesome experimenter, the adolescent who emulates his slightly older associates, or the psychologically dependent man who craves the drug. They find the money somehow to pay for it, as people do for alcohol.

Control by blocking the sources of illicit supply is evidently the ideal. The measures taken have been described in official reports. They bypass the small fry —the peddlers and carriers—and aim at catching the wholesale trafficker; they also try to destroy the hemp crops; thus the United States Bureau of Customs and the corresponding Mexican authorities collaborate in detecting the hemp fields and rooting them out.

A minority of those who discuss prohibition and its problems are concerned with what moral justification the state has for interfering with a citizen's right to do as he pleases as long as he does not infringe the rights of others or harm society. Some stress the alleged detriment caused by cannabis to the user's character and his occupational capacity, thus reducing his social usefulness; others point to injuries caused by his behaviour in driving lorries or cars under the influence of the drug. Some urge that if alcohol and tobacco can be tolerated and taxed there is no logical ground for abstaining from doing likewise with cannabis (on to which, they suggest, an unwarranted moralistic stigma has been pinned); they believe that if a drug, such as alcohol or cannabis, is generally and

readily obtainable in a given society most people learn to use it in moderation, while the psychopathic minority who use it to excess would do so with some available alternative drug anyway. The significant débâcle of alcohol prohibition in the United States has a bearing on the argument for treating cannabis like alcohol. A well established socially permissible drug is evidently ineradicable by total prohibition, whereas a comparative newcomer, like cannabis in Western countries, is a weakling which some suppose might be kept in check by firm action.

At the present time it is widely accepted that dependence on a drug calls for medical treatment. This contention is easily justified in the case of drugs to which a physical dependence may develop. However, in the case of cannabis where the dependence is purely psychological, the issue has been contested. The majority of writers are in favour of psychiatric treatment (provided that the user wants to be treated), combined with social measures of rehabilitation and appropriate social investigation. Broadly, of course, a medical approach is concerned with the welfare of the individual, a social approach is directed more at the protection of society: they complement each other. An antithesis between medical research and social research in this field, or between medical and social treatment, is forced.

BIBLIOGRAPHY

AMPHETAMINES

Effects of Acute Intoxication

Brengelmann, J. C., 1958. D-amphetamine and amytal. I. Effects on memory and expressive movement. II. Effects on certainty and adequacy of certainty in recall and recognition. *J. ment. Sci.*, **104**, 153.

Buffardi, R., 1961. Sul problema dell'attivazione in psicologia clinica. *Acta neurol.*, **16**, 320.

Delay, J., 1949. Les explorations pharmacodynamiques du psychisme: narco-analyse et choc amphétaminique. *Bull. Acad. natn. Méd.*, **133**, 289.

Delay, J., Pichot, P. and Deniker, P., 1950. Action des amphétamines dans les états d'excitation maniaque: quelques effects paradoxaux. *Annls méd.-psychol.*, **108**(2), 194.

Delay, J., *et al.*, 1947. L'emploi de Méthédrine en psychiatrie. L'exploration des mutismes (présentation de malades). *Annls méd.-psychol.*, **105**(2), 50.

Dickins, D. W., Lader, M. H. and Steinberg, H., 1965. Differential effects of two amphetamine-barbiturate mixtures in man. *Br. J. Pharmacol.*, **24**, 14.

Durrant, B. W., 1965. Amphetamine addiction. *Practitioner*, **194**, 649.

Evans, W. O. and Jewett, A., 1962. The effect of some centrally acting drugs on disjunctive reaction time. *Psychopharmacologia*, **3**, 124.

Evans, W. O. and Smith, R. P., 1964. Some effects of morphine and amphetamine on intellectual functions and mood. *Psychopharmacologia*, **6**, 49.

Franchini, C., 1957. Shock anfetaminico e sindromi di arresto psico-motorio. *Neurone*, **5**, 71.

Frankenhaeuser, M. and Post, B., 1965. Objective and subjective performance as influenced by drug-induced variations in activation level. *Stockholm Psychol. Lab. Rep.*, **184**, 1.

Goldberg, L., 1968. Drug abuse in Sweden. *Bull. Narcot.*, **20**(1), 1; **20**(2), 9.

Goldstein, A., Searle, B. W. and Schimke, R. T., 1960. Effects of secobarbital and of d-amphetamine on psychomotor performance of normal subjects. *J. Pharmacol. exp. Ther.*, **130**, 55.

Hawkins, D. R., *et al.*, 1961. A multivariant psychopharmacologic study in normals. *Psychosom. med.*, **23**, 1.

Holliday, A. R., 1966. The effects of d-amphetamine on errors and correct responses of human beings performing a simple intellectual task. *Clin. Pharmac. Ther.*, **7**, 312.

Hubin, P. and Servais, J., 1966. Étude comparative des effets psychophysiologiques de l'amphétamine chez des sujets de race blanche et de race noire. *Psychopharmacologia*, **9**, 118.

Hubin, P. and Servais, J., 1968. Étude des effets subjectifs de l'amphétamine chez l'homme en fonction de la personnalité. *Psychopharmacologia*, **12**, 239.

Kalant, O. J., 1966. *The amphetamines: toxicity and addiction.* (Brookside Monograph No. 5.) Toronto, University of Toronto Press.

Kastenbaum, R., Slater, P. E. and Aisenberg, R., 1964. Toward a conceptual model of geriatric psychopharmacology: an experiment with thioridazine and dextroamphetamine. *Gerontologist*, **4**, 68.

Kenyon, G. Y. and Pronko, N. H., 1960. Dexedrine (d-amphetamine sulfate) and laboratory induced anxiety. *Psychol. Rep.*, **7**, 415.

Legge, D. and Steinberg, H., 1962. Actions of a mixture of amphetamine and a barbiturate in man. *Br. J. Pharmac.*, **18**, 490.

McKenzie, R. E. and Elliott, L. L., 1965. Effects of secobarbital and d-amphetamine on performance during a simulated air mission. *Aerospace Med.*, **35**, 774.

Modell, W. and Hussar, A. E., 1965. Failure of dextroamphetamine sulfate to influence eating and sleeping patterns in obese schizophrenic patients. Clinical and pharmacological significance. *J. Am. med. Ass.*, **193**, 275.

Murray, I. P. C., 1964. The measurement of reaction time in the evaluation of drug action. *Med. J. Aust.*, i, 949.

Panse, F. and Klages, W., 1964. Clinical psychopathologic observations in chronic abuse of ephedrine and related substances. *Arch. Psychiat. Nerven-Krankh.*, **206**, 69.

Pathy, M. S., 1957. Acute amphetamine poisoning. *Br. med. J.*, i, 946.

Pierson, W. R., Rasch, P. J. and Brubaker, M. L., 1961. The effects of amphetamine sulfate and moprobamate on the variability of simple response time. *Sportarztl. Prax.*, **2/3**, 80.

Ross, S., *et al.*, 1962. Drugs and placebos: a model design. *Psychol. Rep.*, **10**, 383.

Servais, J. and Hubin, P., 1964. Étude psychopharmacologique de l'amphétamine et du méprobamate chez l'homme normal. *Int. J. Neuropharmac.*, **3**, 517.

Smith, G. M. and Beecher, H. K., 1964. Drugs and judgment: effects of amphetamine and secobarbital on self-evaluation. *J. Psychol.*, **58**, 397.

Smith, G. M., *et al.*, 1963. Effects of amphetamine and secobarbital on coding and mathematical performance. *J. Pharmac. exp. Ther.*, **141**, 100.

Weiner, H. and Ross, S., 1962. Effects of d-amphetamine sulphate on time and brightness perception in human subjects. *Psychopharmacologia*, **3**, 44.

Weiss, B. and Laties, V. G., 1962. Enhancement of human performance by caffeine and the amphetamines. *Pharmac. Rev.*, **14**, 1.

Weitzner, M., 1965. Manifest anxiety, amphetamine and performance. *J. Psychol.*, **60**, 71.

Zanetti, G., 1950. Lo "schoc anfetaminico": nuova metodo di esplorazione psichiatrica. *G. Psichiat. Neuropatol.*, **78**, 41.

Causes and Modifying Factors

Durrant, B. W., 1965. Amphetamine addiction. *Practitioner*, **194**, 649.

Hawkins, D. R., *et al.*, 1961. A multivariant psychopharmacologic study in normals. *Psychosom. Med.*, **23**, 1.

Lancet, 1964. Amphetamine and delinquency. *Lancet*, ii, 452.

Reed, C. F. and Witt, P. N., 1965. Factors contributing to unexpected reactions in two human drug-placebo experiments. *Confinia psychiat.*, **8**, 57.

Scott, P. D. and Willcox, D. R. C., 1965. Delinquency and the amphetamines. *Br. J. Psychiat.*, **111**, 865.

Prevalence

Abeles, H., *et al.*, 1966. Multiple-drug addiction in New York City in a selected population group. *Publ. Hlth. Rep. Wash.*, **81**, 685.

Fleming, A. S., 1960. Amphetamine drugs. *Publ. Hlth Rep. Wash.*, **75**, 49.

Goldenberg, M. and Caparrós, A., 1961. Intoxicacion por Bencedrinicos. *Acta neuropsiq. argent.*, **7**, 120.

Griffith, J., 1966. A study of illicit amphetamine drug traffic in Oklahoma City. *Am. J. Psychiat.*, **123**, 560.

Journal of the Iowa Medical Society, 1962. The hazards of amphetamine therapy. *J. Iowa St. med. Soc.*, **52**, 671.

McConnell, W. B. and McIlwaine, R. J., 1961. Amphetamine substances and mental illness in Northern Ireland. *Ulster med. J.*, **30**, 31.

Masaki, T., 1956. The amphetamine problem in Japan. In: *Tech. Rep. Ser. World Health Org.*, **102**, p. 14.

Sano, I. and Nagasaka, 1956. Über chronische Weckaminsucht in Japan. *Fortschr. Neurol. Psychiat.*, **24**, 391.

Smith, G. M. and Beecher, H. K., 1964. Drugs and judgment: effects of amphetamine and secobarbital on self-evaluation. *J. Psychol.*, **58**, 397.

Smith, S. N. and Blachly, P. H., 1966. Amphetamine usage by medical students. *J. med. Educ.*, **41**, 167.

Smith, G. M., *et al.*, 1963. Effects of amphetamine and secobarbital on coding and mathematical performance. *J. Pharmac. exp. Ther.*, **141**, 100.

Tatetsu, S., 1960. Pervitin-Psychosen. *Folia psychiat. neurol. jap. Suppl.*, **6**, 25.

Adverse Effects of Misuse

Askevold, F., 1959. The occurrence of paranoid incidents and abstinence delirium in abusers of amphetamine. *Acta psychiat. scand.*, **34**, 145.

Beamish, P. and Kiloh, L. G., 1960. Psychoses due to amphetamine consumption. *J. ment. Sci.*, **106**, 337.

Bell, D. S., 1965. Comparison of amphetamine psychosis and schizophrenia. *Br. J. Psychiat.*, **111**, 701.

Bell, D. S. and Trethowan, W. H., 1961. Amphetamine addiction. *J. nerv. ment. Dis.*, **133**, 489.

Bell, D. S. and Trethowan, W. H., 1961. Amphetamine addiction and disturbed sexuality. *Archs. gen. Psychiat.*, **4**, 74.

Berry, J. N., 1966. Acute myeloblastic leukemia in a benzedrine addict. *Sth. med. J., Nashville*, **59**, 1169.

Brandon, S. and Smith, D., 1962. Amphetamines in general practice. *J. Coll. gen. Practnrs*, **5**, 603.

Breitner, C., 1963. Appetite suppressing drugs as an etiologic factor in mental illness. *Psychosomatics*, **4**, 327.

Connell, P. H., 1958. *Amphetamine psychosis*. London, Chapman.

Connell, P. H., 1962. The amphetamines. *Med. Wld, Lond.*, **96**, 18; 106.

Ellinwood, E. H., 1967. Amphetamine psychosis: I. Description of the individuals and process. *J. nerv. ment. Pis.*, **144**, 273.

Glatt, M. M., 1962. Dependence on sedatives and stimulants. *Br. med. J.*, ii, 673.

Greenburg, H. R. and Lustig, N., 1966. Misuse of dristan inhaler. *N.Y. St. J. Med.*, **66**, 613.

Greenwood, R. and Peachey, R. S., 1957. Acute amphetamine poisoning: an account of three cases. *Br. med. J.*, i, 742.
Griffith, J., 1966. A study of illicit amphetamine traffic in Oklahoma City. *Am. J. Psychiat.*, **123**, 560.
Hampton, W. H., 1961. Observed psychiatric reactions following the use of amphetamine-like substances. *Bull. N.Y. Acad. Med.*, **37**, 167.
Jorgensen, F. and Kodahl, T., 1961. Om ritalinmisbrug. *Ugeskr. Laeg.*, **123**, 1275.
Kalant, O. J., 1966. *The amphetamines: toxicity and addiction.* (Brookside Monograph No. 5). Toronto, University of Toronto Press.
Kramer, J. C., Fischman, V. S. and Littlefield, D. C., 1967. Amphetamine abuse: pattern and effects of high doses taken intravenously. *J. Am. med. Ass.*, **201**, 305.
McConnell, W. B., 1963. Amphetamine substances in mental illnesses in Northern Ireland. *Br. J. Psychiat.*, **109**, 218.
Moss, P. D., 1962. Phenmetrazine and foetal abnormalities. *Br. med. J.*, ii, 1610.
O'Flanagan, P. M. and Taylor, R. B., 1950. A case of recurrent psychosis associated with amphetamine addiction. *J. ment. sci.*, **96**, 1033.
Panse, F. and Klages, W., 1964. Clinical psychopathologic observations in chronic abuse of ephedrine and related substances. *Arch. Psychiat. Nerv-Krankh.*, **206**, 69.
Powell, P. D. and Johnstone, J. M., 1962. Phenmetrazine and foetal abnormalities. *Br. med. J.*, ii, 1327.
Quadbeck, G. and Schmitt, W., 1966. Klinisch-psychopathologische und tierexperimentelle Untersuchungen zur Frage der chronischen Phenmetrazin-Intoxikation. *Arzneimittel-Forsch.*, **16**, 247.
Refshauge, W. D., 1963. Phenmetrazine and trifluoperazine. *Med. J. Aust.*, i, 58.
Richman, E. E., Williams, E. Y. and Brown, R. K., 1961. Acute toxic psychiatric reactions related to amphetamine medication. *Med. Ann. Distr., Columbia.*, **30**, 209.
Tolentino, I. and D'Avossa, B., 1957. Psicosi da amine simpatico-mimetiche. *Archo Psicol. Neurol. Psichiat.*, **18**, 127.
Weiner, I. B., 1964. Differential diagnosis in amphetamine psychosis. *Psychiat. Q.*, **38**, 707.
Welsh, A. L., 1962. *Side effects of anti-obesity drugs.* Springfield, Thomas.
World Health Organization, 1956. [Sixth report of the] Expert Committee on Drugs Liable to Produce Addiction. *Tech. Rep. Ser. Wld. Hlth. Org.*, **102**, 12.
Young, G. G., Simson, C. B. and Frohman, C. E., 1961. Clinical and biochemical studies of an amphetamine withdrawal psychosis. *J. nerv. ment. Dis.*, **132**, 234.
Zalis, E. G. and Pharmley, L. F., 1963. Fatal amphetamine poisoning. *Archs intern. Med.*, **112**, 822.

Benefits and Therapeutic Use

Adamson, G. T. and Finlay, S. E., 1965. The effects of two psycho-stimulant drugs on muscular performance in male athletes. *Ergonomics*, **8**, 237.
Albrinke, M. J., 1963. *Obesity.* In: Cecil and Loeb's *Textbook of medicine*, edited by P. Beeson and W. MacDermott, London, Saunders, p. 1164.

Altschule, M. D., 1963. Amphetamine and performance. *J. Am. med. Ass.*, **185**, 549.

Bischoff, A., 1951. Über eine therapeutische Verwendung der sogenannten "Weck-Amine" in der Behandlung schizophrener Erregungszustande. *Mschr. Psychiat. Neurol.*, **121**, 329.

Bradley, C., 1950. Benzedrine and dexedrine in the treatment of children's behaviour disorders. *Pediatrics*, **5**, 24.

British Medical Journal, 1963. Amphetamines. *Br. med. J.*, i, 173.

Burks, H. F., 1964. Effects of amphetamine therapy of hyperkinetic children. *Archs. gen. Psychiat.*, **11**, 604.

Cauffman, W. J. and Pauley, W. G., 1961. Obesity and emotional status. *Penn. med. J.*, **64**, 505.

Conners, C. K., Eisenberg, L. and Barcai, A., 1967. Effect of dextroamphetamine on children. *Archs. gen. Psychiat.*, **17**, 478.

Conners, C. K., Eisenberg, L. and Sharpe, L., 1964. Effects of methylphenidate (Ritalin) on paired-associate learning and Porteus Maze performance in emotionally disturbed children. *J. consult. Psychol.*, **28**, 14.

Duckworth, H. C., 1940. Benzedrine in the treatment of morphine addiction. *Br. med. J.*, ii, 628.

Eisenberg, L., *et al.*, 1963. A psychopharmacologic experiment in a training school for delinquent boys: methods, problems, findings. *Am. J. Orthopsychiat.*, **33**, 431.

Fann, W. E., 1965. Use of methylphenidate to counteract acute dystonic effects of phenothiazines. *Am. J. Psychiat.*, **122**, 1293.

Fish, C. H. and Bowling, E., 1962. Effects of amphetamines on speech defects in the mentally retarded. *Calif. Med.*, **96**, 109.

Gottleib, J. S., 1949. The use of sodium amytal and benzedrine sulfate in the symptomatic treatment of depressions. *Dis. nerv. Syst.*, **10**, 50.

Hare, E. H., Dominian, J. and Sharpe, L., 1962. Phenelzine and dexamphetamine in depressive illness. A comparative trial. *Br. med. J.*, i, 9.

Hare, E. H., McCance, C. and McCormick, W. O., 1964. Imipramine and "drinamyl" in depressive illness. A comparative trial. *Br. med. J.*, i, 818.

Imlah, N. W., 1961. Narcolepsy in identical twins. *J. Neurol. Neurosurg. Psychiat.*, **24**, 158.

Lancet, 1947. A versatile remedy. *Lancet*, i, 567.

Lancet, 1965. Amphetamine. *Lancet*, i, 1374.

Leake, C. D., 1958. *The amphetamines: the actions and uses.* Springfield, Thomas.

McConnell, T. R. W., *et al.*, 1964. Studies in activity level: VII. Effects of amphetamine drug administration on the activity level of retarded children. *Am. J. ment. Defic.*, **68**, 647.

McKenzie, R. E. and Elliott, L. L., 1965. Effects of secobarbital and d-amphetamine on performance during a simulated air mission. *Aerospace Med.*, **36**, 774.

Nabarro, J. D. N., 1950. Use of intravenous amphetamine sulphate in acute barbiturate poisoning. *Br. med. J.*, ii, 924.

Nash, H., 1962. Psychologic effects of amphetamines and barbiturates. *J. nerv. ment. Dis.*, **134**, 203.

Pierson, W. R., Rasch, P. J. and Brubaker, M. L., 1961. The effects of amphetamine sulfate and meprobamate on the variability of simple response time. *Sportarzl. Prax.*, **2/3**, 80.
Practitioner, 1964. Dexamphetamine compared with an inactive placebo in depression. (General practitioner clinical trials). *Practitioner*, **192**, 151.
Rudolf, G. de M. The treatment of depression with desoxyephedrine (methedrine). *J. ment. Sci.*, 1949, **95**, 920.
Smith, G. M., Weitzner, M. and Beecher, H. K., 1963. Increased sensitivity of measurement of drug effects in expert swimmers. *J. Pharmac. exp. Ther.*, **139**, 114.
Smith, S. N. and Blachly, P. H., 1966. Amphetamine usage by medical students. *J. med. Educ.*, **41**, 167.
Swanson, D. W. and Smith, J. A., 1961. The use of stimulating drugs. *Am. J. Psychiat.*, **118**, 419.
Weiss, B. and Laties, V. G., 1962. Enhancement of human performance by caffeine and the amphetamines. *Pharmac. Rev.*, **14**, 1.
Welsh, A. L., 1962. *Side effects of anti-obesity drugs*. Springfield, Thomas.
Zrull, J. P., *et al.*, 1963. A comparison of chlordiazepoxide, d-amphetamine, and placebo in the treatment of hyperkinetic syndrome in children. *Am. J. Psychiat.*, **120**, 590.
Zrull, J. P., *et al.*, 1964. A comparison of diazepam, d-amphetamine and placebo in the treatment of the hyperkinetic syndrome in children. *Am. J. Psychiat.*, **121**, 388.

Tolerance and Dependence

Askevold, F., 1959. The occurrence of paranoid incidents and abstinence delirium in abusers of amphetamine. *Acta psychiat. scand.*, **34**, 145.
Binder, H., 1945. 3. Kriminalität infolge Pervitinmissbrauchs. *Schweizer Arch. Neurol. Psychiat.*, **55**, 243.
Bonhoff, G. and Lawrenz, H., 1954. *Über Weckamine* (*Pervitin and Benzedrin*), Berlin, Springer.
Boor, W. de., 1956. *Pharmakopsychologie und Psychopathologie*. Berlin, Springer.
Brandon, S., 1963. Addiction to amphetamines. *Br. med. J.*, ii, 1204.
Brandon, S. and Smith, D., 1962. Amphetamines in general practice. *J. Coll. gen. Practnrs.*, **5**, 603.
British Medical Journal, 1963. Addiction to amphetamines. *Br. med. J.*, ii, 399.
Connell, P. H., 1958. *Amphetamine psychosis*. London, Chapman.
Goldberg, L., 1968. Drug abuse in Sweden. *Bull. Narcot.*, **20**(1), 1; **20**(2), 9.
Grahn, H. V., 1958. Amphetamine addiction and habituation. *Am. Practnr. Dig. Treat.*, **9**, 387.
Greenburg, H. R. and Lustig, N., 1966. Misuse of dristan inhaler. *N.Y. St. J. Med.*, **66**, 613.
Jorgensen, F. and Kodahl, T., 1961. Om ritalinmisbrug. *Ugeskr. Laeg.*, **113**, 1275.
Journal of Iowa Medical Society, 1962. The hazards of amphetamine therapy. *J. Iowa St. med. Soc.*, **52**, 671.
Kalant, O. J., 1966. *The amphetamines: toxicity and addiction* (Brookside Monograph No. 5). Toronto, University of Toronto Press.

Keyserlingk, H., 1950. Pervitin. *Psychiatric Neurol. med. Psychol.*, **2**, 1.
Knapp, P. H., 1952. Amphetamine and addiction. *J. nerv. ment. Dis.*, **115**, 406.
Kramer, J. C., Fischman, V. S. and Littlefield, D. C., 1967. Amphetamine abuse; pattern and effects of high doses taken intravenously. *J. Am. med. Ass.*, **201**, 305.
Lancet, 1964. Amphetamine and delinquency. *Lancet*, ii, 452.
Leake, C. D., 1958. *The amphetamines: the actions and uses.* Springfield, Thomas.
Lemere, F., 1966. The danger of amphetamine dependency. *Am. J. Psychiat.*, **123**, 569.
Myers, W. H. and Law, E., 1963. Addiction to amphetamine. *Br. med. J.*, ii, 1536.
Nandelstadh, O. W. von, 1951. On benzedrine psychoses. *Acta psychiat. scand. Suppl.*, **60**, 164.
Noda, H., 1966. *The problem of amphetamine abuse in Japan.* In: *The amphetamines: toxicity and addiction*, edited by O. J. Kalant (Brookside Monograph No. 5). Toronto, University of Toronto Press, p. 102.
Nyswander, M., 1959. *Drug addictions.* In: *American handbook of psychiatry*, edited by S. Arieti, Vol. 1. New York, Basic Books, p. 614.
Oswald, I. and Thacore, V. R., 1963. Amphetamine and phenmetrazine addiction. Physiological abnormalities in the abstinence syndrome. *Br. med. J.*, ii, 427.
Pollock, B., 1964. Report of an unusually large dosage of methylphenidate hydrochloride. *Am. J. Psychiat.*, **121**, 189.
Rosenberg, D. B., *et al.*, 1963. Observations on direct and cross tolerance with LSD and dextroamphetamine in man. *Psychopharmacologia*, **5**, 1.
Scott, P. D. and Willcox, D. R. C., 1965. Delinquency and the amphetamines. *Br. J. Psychiat.*, **111**, 865.
Weiss, B. and Laties, V. G., 1962. Enhancement of human performance by caffein and the amphetamines. *Pharmacol. Rev.*, **14**, 1.
Wilson, C. W. M., 1965. Diagnosis of amphetamine addiction. *Br. med. J.*, i, 659.
Young, G. G., Simson, C. B. and Frohman, C. E., 1961. Clinical and biochemical studies of an amphetamine withdrawal psychosis. *J. nerv. ment. Dis.*, **132**, 234.
Zalis, E. and Pharmley, L. F., 1963. Fatal amphetamine poisoning. *Archs. intern. med.*, **112**, 822.

Progression

Bonhoff, G. and Lewrenz, H., 1954. *Über Weckamine (pervitin und Benzedrin).* Berlin, Springer.
Goldberg, L., 1968. Drug abuse in Sweden. *Bull. Narcot.*, **20**(1), 1; **20**(2), 9.
Kramer, J. C., Fischman, V. S. and Littlefield, D. C., 1967. Amphetamine abuse: pattern and effects of high doses taken intravenously. *J. Am. med. Ass.*, **201**, 305.
Legge, D. and Steinberg, H., 1962. Actions of a mixture of amphetamine and a barbiturate in man. *Br. J. Pharmacol.*, **18**. 490.
Masaki, T., 1956. The amphetamine problem in Japan. *Tech. Rep. Ser. Wld. Hlth. Org.*, **102**, 14.

Nyswander, M., 1959. *Drug addictions.* In: *American handbook of psychiatry*, edited by S. Arieti. Vol. 1. New York, Basic Books, p. 614.

Legislation

British Medical Journal, 1965. Loophole for pep pills? *Br. med. J.*, i, 739.
Bundock, J. B., 1962. Canada's new controls of the barbiturates and the amphetamines. *Mes. serv. J. Can.*, **18**, 464.
Goldberg, L., 1968. Drug abuse in Sweden. *Bull. Narcot.*, **20**(1), 1; **20**(2), 9.
Johnson, J. and Milner, G., 1965. Diagnosis of amphetamine addiction. *Br. med. J.*, i, 589.
Kalant, O. J., 1966. *The amphetamines: toxicity and addictions* (Brookside Monograph No. 5). Toronto, University of Toronto Press.
Masaki, T., 1956. The amphetamine problem in Japan. *Tech. Rep. Ser. Wld. Hlth. Org.*, **102**, 14.

BARBITURATES

Adams, B. G., *et al.*, 1966. Patients receiving barbiturates in an urban general practice. *J. Coll. Gen. Practit.*, **12**, 24.
Armitage, G. H. and Sim, M., 1960. Barbiturate addiction and sensitivity. *Br. J. med. Psychol.*, **33**, 149.
Berger, F. M., 1967. Drugs and suicide in the United States. *Clin. Pharmac. Ther.*, **8**, 219.
Bewley, T., 1966. Recent changes in the pattern of drug abuse in the United Kingdom. *Bull. Narcot.*, **18**(4), 1.
Blachly, P. H., 1964. Procedure for withdrawal of barbiturates. *Am. J. Psychiat.* **120**, 894.
Boor, W. de, 1956. *Pharmakopsychologie und Psychopathologie.* Berlin, Springer, p. 51.
Brazelton, T. B., 1961. Psychophysiologic reactions in the neonate. II. Effect of maternal medication on the neonate and his behaviour. *J. Pediat.*, **58**, 513.
Brilmayer, H., Wieck, H. H. and Picka, N., 1962. Verlaufsbeobachtungen bei Vergiftungen mit Barbituraten. *Dt. med. Wschr.*, **87**, 1572.
Brooke, E. M. and Glatt, M. M., 1964. More and more barbiturates. *Med. Sci. Law*, **4**, 277.
Bulletin on Narcotics, 1956. Illicit traffic in narcotics, barbiturates and amphetamines in the United States. Report to the Committee on Ways and Means of the House of Representatives of the Congress of the United States of America from the Sub-Committee on Narcotics. *Bull. Narcot.*, **8**(3), 13–18.
Bulletin on Narcotics, 1957. The problem of barbiturates in the United States of America. *Bull. Narcot.*, **9**(2), 15.
Bulletin on Narcotics, 1967. The road to controls: barbiturates, amphetamines, tranquillizers and hallucinegens. *Bull. Narcot.*, **19**(1), 15.
Busch, K. T., 1960. Veranderungen am Gehirn bei chronischem Schlafmittelabusus. *Psychiat. Neurol. med. Psychol.*, **12**, 103.
Campanini, N., 0000. The barbiturates, amphetamines and hallucinogens, and their control in Switzerland. *Bull. Narcot.*, **19**(2), 13.
Davis, H., 1957. The prescribing of barbiturates. *Br. J. Addict.*, **53**, 101.

Deberdt, R., 1961. Sur un cas de neuropathie barbiturique. *J. Sciences med. Lille*, **79**, 294.

Essig, C. F., 1968. *Additction to barbiturate and nonbarbiturate sedative drugs.* In: *The addictive states. Proceedings of the Association, December* 2 *and* 3, 1966 (Research Publications Association for Research in Nervous and Mental Disease, Vol. XLVI, editor A. Wikler). Baltimore, Williams and Wilkins.

Fabiani, P., 1959. Sindrome di delirium tremens da sospensione brusca di (etil(1-metil-butil)barbiturato di sodio) in tossicomane. *Boll. Soc. med. chir. Pisa*, **27**, 333.

Fort, J., 1964. The problem of barbiturates in the United States of America. *Bull. Narcot.*, **16**(1), 17.

Fraser, H. F., *et al.*, 1954. Chronic barbiturate intoxication. *Archs intern. Med.*, **94**, 34.

Fraser, H. F., *et al.*, 1953. Death due to withdrawal of barbiturates. *Ann. intern. Med.*, **38**, 1319–1325.

Fraser, H. F., *et al.*, 1958. Degree of physical dependence induced by secobarbital or pentobarbital. *J. Am. med. Ass.*, **166**, 126.

Gardner, A. J., 1967. Withdrawal fits in barbiturate addicts. *Lancet*, ii, 337.

Gillespie, R. D., 1934. On the alleged dangers of the barbiturates. *Lancet*, i, 337.

Glatt, M. M., 1962. The abuse of barbiturates in the United Kingdom. *Bull. Narcot.*, **14**(2), 19.

Graham, J. D. P., 1958. Acute barbitone and bromide poisoning with unusual features. *Br. med. J.*, ii, 1275.

Gupta, R. C. and Kofoed, J., 1966. Toxicological statistics for barbiturates, other sedatives and tranquillizers in Ontario: a 10-year survey. *Can. med. Ass. J.*, **94**, 863.

Hamburger, E., 1965. Identification and treatment of barbiturate abusers. *J. Am. med. Ass.*, **193**, 393.

Hormia, A., 1957. Psychose épileptique caracterisée par une panique homosexuelle dans la phase d'abstinence consécutive a un barbiturisme chronique. Exemple de concours de facteurs psychogènes et somatiques. *Encéphale*, **46**, 245.

Hunter, R. A., 1957. The abuse of barbiturates and other sedative drugs with special reference to psychiatric patients. *Br. J. Addict.*, **53**, 93.

Isbell, H., 1956. Abuse of barbiturates. *J. Am. med. Ass.*, **162**, 660.

Isbell, H., 1967. Abuse of barbiturates. *Bull. Narcot.*, **9**(2), 14.

Isbell, H., *et al.*, 1950. Chronic barbiturate intoxication. *Archs Neurol. Psychiat., Chicago*, **64**, 1.

Isbell, H. and Fraser, H. F., 1950. Addiction to analgesics and barbiturates. *Pharmac. Rev.*, **2**, 355.

Journal of the American Medical Association, 1959. Medical guide for physicians in determining fitness to drive a motor vehicle. *J. Am. med. Ass.*, **169**, 1195.

Journal of the American Medical Association, 1965. Dependence on barbiturates and other sedative drugs. AMA Committee on Alcoholism and Addiction and Council on Mental Health. *J. Am. med. Ass.*, **193**, 673.

Kåss, E., Retterstøl, N. and Sirnes, T. B., 1958. Barbituratintoksikasjoner som problem i en indremedisinsk avdeling med fast tilknyttet psykiater. *Tidsskr. norske Laegeforen.*, **78**, 334.

Lancet, 1967. Barbiturate poisoning. *Lancet*, i, 200.

Locket, S., 1957. The abuse of barbiturates. *Br. J. Addict.*, **53**, 105.
McBay, A. J., 1965. Barbiturate poisoning. *New Engl. J. Med.*, **273**, 38.
McGuiness, B. W. and Roberts, F. J., 1960. Megimated barbiturates. *Br. med. J.*, ii, 996.
Mann, J., 1961. Acute porphyria provoked by barbiturates given with electroshock therapy. *Am. J. Psychiat.*, **118**, 509.
Maurer, D. W. and Vogel, V. H., 1962. *Narcotics and narcotic addiction.* Springfield, Thomas.
Pohlisch, K., 1928. Über psychische Reaktionsformen bei Arzneimittelvergiftungen. *Mschr. Psychiat. Neurol.*, **69**, 293.
Roger, J., Toga, M., Mouren, P. and Castant, H., 1959. Constations anatomiques dans un cas d'epilepsie du sevrage après dure de sommeil. *Revue Neurol.*, **100** 741.
Stechler, G., 1964. Newborn attention as affected by medication during labor. *Science*, **144**, 315.
Tatum, A. L., 1939. The present status of the barbiturate problem. *Physiol. Rev.*, **19**, 472.
Wikler, A., 1957. *The relation of psychiatry to pharmacology.* Baltimore, Williams and Wilkins.
Willcox, W., *et al.*, 1934. Discussion on the uses and dangers of hypnotic drugs other than alkaloids. *Proc. roy. soc. Med.*, **27**, 489.
World Health Organization, 1964. W.H.O. Expert Committee on Addiction Producing Drugs, thirteenth report. *Tech. Rep. Ser. Wld. Hlth. Org.*, **273**.

LSD

Effects

Alnaes, R., 1964. Therapeutic application of the change of consciousness produced by psycholita (LSD, psilocybin, etc.). The psychedelic experience in the treatment of neurosis. *Acta psychiat. scand., Suppl.*, **180**, 397.
Amarel, M. and Cheek, F. E., 1965. Some effects of LSD-25 on verbal communication. *J. abnorm. Psychol.*, **70**, 453.
Anastasopoulos, G. and Photiades, H., 1962. Effects of LSD-25 on relatives of schizophrenic patients. *J. ment. Sci.*, **108**, 95.
Aronson, H. and Klee, G. D., 1960. Effect of lysergic acid diethylamide (LSD-25), on impulse control. *J. nerv. ment. Dis.*, **131**, 536.
Balestrieri, A., 1961. *Patologia mentale et farmacologia.* Padova, Cedam.
Balestrieri, A., 1961. *Some aspects of the sensitivity to hallucinogenic drugs.* In: *Neuro-Psychopharmacology, Volume* 2. *Proceedings of the second meeting of the Collegium Internationale Neuro-Psychopharmacologicum*, Basle, 1960, edited by E. Rothlin. Amsterdam, Elsevier, p. 44.
Barron, F., Jarvik, M. E. and Bunnell, S., 1964. The hallucinogenic drugs. *Scient. Am.*, **210**, 29.
Benda, P. and Orsini, F., 1961. *Fluctuations du niveau d'efficience sous LSD*-25. In: *Neuro-Psychopharmacology, Volume* 2. *Proceedings of the second meeting of the Collegium Internationale Neuro-Psychopharmacologicum*, Basle, 1960, edited by E. Rithlin. Amsterdam, Elsevier, p. 339.

Bensoussan, P.-A., Joannidès, A.-A. and Soubrier, J.-P., 1966. Note sur quelques accidents de l'usage incontrôle des psycho-dysleptiques. *Annls. méd-psychol.* **124**(2), 90.

Blum, R., *et al.*, 1965. *Utopiates: the use and users of LSD* 25. London, Tavistock Publications.

Bowers, M., *et al.*, 1967. Dynamics of psychedelic drug abuse. A clinical study. *Archs gen. Psychiat.*, **16**, 150.

Brattemo, C. E. and Lassenius, B., 1963. Lysergsyradietylamid en klinisk och psykoyogist studie. *Nord. Med.*, **69**, 193.

Chandler, A. L. and Hartman, M. A., 1960. Lysergic acid diethylamide (LSD-25) as a facilitating agent in psychotherapy. *Archs gen. Psychiat.*, **2**, 286.

Cheek, F., 1963. Exploratory study of drugs and social interaction. *Archs gen. Psychiat.*, **9**, 566.

Chessick, R. D., Haertzen, C. A. and Wikler, A., 1964. Tolerance to LSD-25 in schizophrenic subjects. *Archs gen. Psychiat.*, **10**, 653.

Cohen, S., 1964. *The beyond within: the LSD story.* New York, Athenaeum.

Cohen, S., 1966. A classification of LSD complications. *Psychosomatics*, **7**, 182.

Cohen, S., 1967. Psychotomimetic agents. *Ann. Rev. Pharmacol.*, **7**, 301.

Cohen, S. and Ditman, K. S., 1963. Prolonged adverse reactions to lysergic acid diethylamide. *Archs gen. Psychiat.*, **8**, 475.

Cole, J. O. and Katz, M. M., 1964. The psychotomimetic drugs: an overview. *J. Am. med. Ass.*, **187**, 758.

Delay, J. and Benda, P., 1958. L'experience lysergique: LSD-25; à propos de 75 observations cliniques. *Encéphale*, **47**, 169; and 309.

DiMascio, A., Rinkel, M. and Leiberman, J., 1962. *Personality and psychotomimetic drugs.* In: *Proceedings of the Third World Conference of Psychiatry.* Toronto, University Press, vol. 2, p. 933.

Durand, V.-J., 1960. Diethylamide de l'acide lysergique et psychiatrie. *Annls. méd.-psychol.*, **118**(i), 401.

Eggert, D. C. and Shagass, C., 1966. Clinical prediction of insightful response to a single large dose of LSD. *Psychopharmacologia*, **9**, 340.

Fordham, M., 1963. *Analytic observations on patients using hallucinogenic drugs* In: *Hallucinogenic drugs and their psychotherapeutic use. Proceedings of the Quarterly Meeting of the Royal Medico-Psychological Association, London, February* 1961, edited by R. Crocket, R. A. Sandison and A. Walk. London, H. K. Lewis, p. 125.

Goldberger, L., 1966. Cognitive test performance under LSD-25, placebo and isolation. *J. nerv. ment. Dis.*, **142**, 4.

Guedes, P. L., 1961. Experience with lysergic acid diethylamide (LSD-25). *Archos Neurol. Psiquiat., Habana*, **19**, 28.

Haase, H.-J., 1957. Das Psychotikum "Lysergsäurediäthylamid". *Fortschr. Neurol. Psychiat.*, **25**, 546.

Harman, W. W., *et al.*, 1966. Psychedelic agents in creative problem solving: a pilot study. *Psychol. Rep.*, **19**, 211.

Hollister, L. E., 1964. Chemical psychoses. *Ann. Rev. Med.*, **15**, 203.

Honigfeld, G., 1965. Temporal effects of LSD-25 and epinephrine on verbal behaviour. *J. abnorm. Psychol.*, **70**, 303.

Horackova, E. and Vojtechovsky, M., 1960. Time perception in experimental LSD-25 psychoses. *Cesk. Psychiat.*, **56**, 303.

Hyde, R. W., 1960. *Psychological and social determinants of drug action.* In: *The dynamics of psychiatric drug therapy*, edited by G. S. Sarwer-Foner. Springfield, Ill., Thomas, p. 297.

Isbell, H., *et al.*, 1961. Cross tolerance between LSD and psilocybin. *Psychopharmacologia*, **2**, 147.

Isbell, H., *et al.*, 1964. *Tolerance and cross-tolerance to scopolamine N-ethyl-3-piperidyl benzylate* (*JB*-318) *and LSD*-25. In: *Neuro-Psychopharmacology, Volume* 3. *Proceedings of the third meeting of the Collegium Internationale Neuro-Psychopharmacologicum, Munich, September* 1962, edited by P. B. Bradley, F. Flügel and P. H. Hoch. Amsterdam, Elsevier, p. 440.

Katz, M. M., Waskow, I. E. and Olsson, J., 1968. Characterizing the psychological state produced by LSD. *J, abnorm. Psychol.*, **73**, 1.

Keniston, K., 1965. *The uncommitted; alienated youth in American society.* New York, Harcourt, Brace.

Kenna, J. and Sedman, G., 1964. Subjective experience of time during lysergic acid diethylamide (LSD-25) intoxication. *Psychopharmacologia*, **5**, 280.

Klee, G. D., 1963. Lysergic acid diethylamide (LSD-25) and ego functions. *Archs gen. Psychiat.*, **8**, 461.

Klee, G. D., *et al.*, 1961. The influence of varying dosage on the effects of lysergic acid diethylamide (LSD-25) in humans. *J. nerv. ment. Dis.*, **132**, 404.

Klerman, G. L., 1961. *The influence of personality factors on phrenotropic agent effects.* In: *Transactions of the 6th Research Conference on Cooperative Chemotherapy Studies in Psychiatry and Broad Research Approaches to Mental Illness.* 27, 28 and 29 March, 1961, Washington, D.C. Department of Medicine and Surgery, Veterans Administration, p. 339.

Korngold, M., 1963. LSD and the creative experience. *Psychoanal. Rev.*, **50**, 682.

Krus, D. M. and Wapner, S., 1962. Effect of LSD on pace of performing a variety of tasks. *Percept. mot. Skills*, **14**, 255.

Krus, D. M., *et al.*, 1963. Differential behavioral responsivity to LSD-25. *Archs gen. Psychiat.*, **8**, 557.

Kuramochi, H., 1961. Psychopathological study of experimental psychosis induced by LSD-25. 1. Outline of LSD-symptoms in normal subjects. *Psychiat. Neurol. Jap.*, **63**, 91.

Kuramochi, H. and Takahashi, R., 1964. Psychopathology of LSD intoxication. *Archs gen. Psychiat.*, **11**, 151.

Lennard, H. L., 1964. *A proposed program of research in sociopharmacology.* In: *Psychobiological approaches to social behaviour*, edited by P. H. Leiderman and D. Shapiro. London, Tavistock, p. 127.

Lienert, G. A., 1966. Mental age regression induced by lysergic acid diethylamide. *J. Psychol.*, **63**, 3.

Linton, H. B. and Langs, R. J., 1962. Subjective reactions to lysergic acid diethylamide (LSD-25). *Archs gen. Psychiat.*, **6**, 352.

Linton, H. B., Langs, R. J. and Paul, I. H., 1964. Retrospective alterations of the LSD-25 experience. *J. nerv. ment. Dis.*, **138**, 409.

Ludwig, A. M. and Levine, J., 1965. Patterns of hallucinogenic drug abuse. *J. Am. med. Ass.*, **191**, 92.

McGlothlin, W. H., Cohen, S. and McGlothlin, M. S., 1964. Short-term effects of LSD on anxiety attitudes and performance. *J. nerv. ment. Dis.*, **139**, 266.

Mogar, R. E. and Savage, C., 1964. Personality change associated with psychedelic (LSD) therapy: a preliminary report. *Psychotherapy: Theory, Res. and Practice*, **1**, 154.

Mortimer, R., 1963. In: *Hallucinogenic drugs and their psychotherapeutic use. Proceedings of the Quarterly Meeting of the Royal Medico-Psychological Association in London, February* 1961, edited by R. Crocket, R. A. Sandison and A. Walk. London, H. K. Lewis, p. 167.

Muñoz, L. and Marconi, J., 1966. [Effects of LSD-25 according to the dose and to the degree of sensory deprivation.] *Acta psiquiat. psicol. Am. Lat.*, **12**, 144.

Netz, B., Jonsson, C.-O. and Bergqvist, S., 1963. Effects of lysergic acid diethylamide (LSD-25) on normal subjects in a schizophrenia-discriminating test battery. *Scand. J. Psychol.*, **4**, 143.

Pauk, Z. D. and Shagass, C., 1961. Some test findings associated with susceptibility to psychosis induced by lysergic acid diethylamide. *Compreh. Psychiat.*, **2**, 188.

Paul, I. H., 1964. The effects of a drug-induced alteration in state of consciousness on retention of drive-related verbal material. *J. nerv. ment. Dis.*, **138**, 367.

Paul, I. H., Langs, R. J. and Barr, H. L., 1965. Individual differences in the recall of a drug experience. *J. nerv. ment. Dis.*, **140**, 132.

Pollard, J. C., *et al.*, 1965. *Drugs and phantasy: the effects of LSD, psilocybin and sernyl on college students.* Boston, Little, Brown.

Reed, C. F. and Witt, P. N., 1965. Factors contributing to unexpected reactions in two human drug-placebo experiments. *Confinia psychiat.*, **8**, 57.

Rinkel, M., *et al.*, 1961. *Personality patterns and reactions to psilocybine.* In: *Neuro-Psychopharmacology, Volume* 2. *Proceedings of the second meeting of the Collegium Internationale Neuropsycho-pharmacologicum*, Basle, July 1960, edited by E. Rothlin. Amsterdam, Elsevier, p. 273.

Salvatore, S., 1960. Some related factors of the LSD 25 reaction. *Psychiat. Q.*, **34**, 236.

Savage, C., 1957. The resolution and subsequent remobilization of resistance by LSD in psychotherapy. *J. nerv. ment. Dis.*, **125**, 434.

Savage, C., 1962. LSD, alcoholism and transcedence. *J. nerv. ment. Dis.*, **135**, 429.

Sedman, G. and Kenna, J. C., 1964. The occurrence of depersonalization phenomena under LSD. *Psychiatria Neurol.*, **147**, 129.

Sedman, G. and Kenna, J. C., 1965. The use of LSD-25 as a diagnostic aid in doubtful cases of schizophrenia. *Br. J. Psychiat.*, **111**, 96.

Sherwood, J. N., Stolaroff, M. J. and Harman, W. W., 1962. The psychedelic experience: a new concept in psychotherapy. *J. Neuropsychiat.*, **4**, 69.

Silverstein, A. B. and Klee, G. D., 1960. The effect of lysergic acid diethylamide on dual pursuit performance. *J. clin. exp. Psychopath.*, **21**, 300.

Sjoberg, B. M. and Hollister, L. E., 1965. The effects of psychotomimetic drugs on primary suggestibility. *Psychopharmacologia*, **8**, 251.

Spencer, A. M., 1963. *Psychotherapy with hallucinogens: a clinical report with special reference to the revival of emotional phases of childhood.* In: *Hallucinogenic drugs and their psychotherapeutic use. Proceedings of the Quarterly Meeting of the Royal Medico-Psychological Association, London, February 1961*, edited by R. Crocket, R. A. Sandison and A. Walk. London, H. K. Lewis, p. 61.

Terrill, J., 1962. The nature of the LSD experience. *J. nerv. ment. Dis.*, **135**, 425.

Unger, S. M., 1963. Mescaline, LSD, psilocybin, and personality change: a review. *Psychiatry*, **26**, 111.

Wikler, A., *et al.*, 1965. Reaction time ("mental set") in control and chronic schizophrenic subjects and in postaddicts under placebo, LSD-25, morphine, pentobarbital and amphetamine. *Psychopharmacologia*, **7**, 423.

Wilkins, B., Malitz, S. and Esecover, H., 1962. Clinical observations of simultaneous hallucinogen administration in identical twins. *Am. J. Psychiat.*, **118**, 815.

Wolbach, A. B., Miner, E. J. and Isbell, H., 1962. Comparison of psilocin with psilocybin, mescaline and LSD-25. *Psychopharmacologia*, **3**, 219.

Ziolko, H. U., 1961. Subjektive Faktoren der Psychiatrischen Pharmakotherapie. *Dt. med. J.*, **12**, 533.

Ziolko, H. U., 1966. Persönlichkeitsabhängige Veränderungen in der experimentellen Psychose durch Lysergsäurediäthylamid. *Arzneimittel-Forsch.*, **16**, 249.

Use in Treatment of Adults

Abramson, H. A., 1966. LSD in psychotherapy and alcoholism. *Am. J. Psychother.*, **20**, 415.

Allhadeff, B. W., 1963. Les effets psychotomimétiques du LSD et de la psilocybine dans l'exploration clinique de la personalité. *Schweiz. Arch. Neurol. Psychiat.*, **92**, 238.

Anderson, H., Kristensen, K. K. and Knudsen, K. P., 1961. LSD-behandling. Psykoterapi ved hjaelp af lysergyre-diaetyl-amid. *Ugeskr. Laeg.*, **123**, 1449.

Arendsein-Hein, G. W., 1963. *LSD in the treatment of criminal psychopaths.* In: *Hallucinogenic drugs and their psychotherapeutic use. Proceedings of the Royal Medico-Psychological Association, February 1961*, edited by R. Crocket, R. A. Sandison and A. Walk. London, H. K. Lewis, p. 101.

Arendsen-Hein, G. W., 1963. Treatment of the neurotic patient, resistant to the usual techniques of psychotherapy, with special reference to LSD. *Acta Psychother., Suppl.*, **4**, 50.

Atchkova, M., 1965. [Mental reactions to lysergic acid diethylamide in oligophrenia in relation to the patient's age] (in Russian). *Zh. Nevropat. Psikhiat.*, **65**, 1840.

Baker, E. F. W., 1964. Use of lysergic acid diethylamide (LSD-25) in psychotherapy. *Can. med. Ass. J.*, **91**, 1200.

Ball, J. R. and Armstrong, J. J., 1961. The use of LSD-25 (d-lysergic acid diethylamide) in the treatment of the sexual perversions. *Can. Psychiat. Ass. J.*, **6**, 231.

Barolin, G. S., 1961. Erstes Europäisches symposium für psychotherapie under LSD-25, Gottingen, November 1960. *Wien. med. Wschr.*, **111**, 466.

Belden, E. and Hitchen, R., 1963. The identification and treatment of an early deprivation syndrome in alcoholics by means of LSD-25. *Am. J. Psychiat.*, **119**, 985.

Benton, A. J., 1964. The influence of LSD-25 research on an alcoholic psychosis, *Am. J. Psychiat.*, **120**, 907.

Borenstein, P., *et al.*, 1965. Epreuve à la diéthylamide de l'acide lysergique et therapeutiques psychotropes: étude clinique et psychologique. *Annals. méd,-psychol.*, **123**(ii), 223.

British Medical Journal, 1963. Lysergic acid in treatment of neuroses. *Br. med. J.*, ii, 106.

Cameron, K., 1963. *Some experiences with LSD in the treatment of adolescent boys.* In: *Hallucinogenic drugs and their psychotherapeutic use. Proceedings of the Royal Medico-Psychological Association, February 1961*, edited by R. Crocket, R. A. Sandison and A. Walk. London, H. K. Lewis, p. 107.

Cheek, F. E., *et al.*, 1966. Observations regarding the use of LSD-25 in the treatment of alcoholism. *J. Psychopharmac.*, **1**, 56.

Ditman, K. S., 1963. Psychotomimetics: pharmacodynamic and psychotherapeutic properties. *Proc. West Pharmacol. Soc.*, **6**, 13.

Ditman, K. S., Hayman, M. and Whittlesey, J. R. B., 1962. Nature and frequency of claims following LSD. *J. nerv. ment. Dis.*, **134**, 346.

Eisner, B. G., 1963. *The influence of LSD on unconscious activity.* In: *Hallucinogenic drugs and their psychotherapeutic use. Proceedings of the Royal Medico-Psychological Association, February* 1961, edited by R. Crocket, R. A. Sandison and A. Walk. London, H. K. Lewis, p. 141.

Fontana, A. E., 1961. El uso clinico de las drogas alucinogenas. *Acta neuropsiq. argent.*, **7**, 94.

Geert-Jörgensen, E., 1961. Model-psykoser og lysergsyre-diaetyl-amid behandling. *Ugeskr. Laeg.*, **123**, 1452.

Geert-Jörgensen, E., *et al.*, 1965. LSD treatment. Experience gained within a three-year period. *Acta psychiat. scand., Suppl.*, **180**, 373.

Grinker, R. R., 1963. Lysergic acid diethylamide. *Archs gen. Psychiat.*, **8**, 425.

Gucker, D. K., 1963. Combining external and internal symbolization in the LSD episode. *J. Psychol.*, **55**, 401.

Hausner, M. and Dolezal, V., 1963. Catamnestic evaluation of psychotherapeutic results with the use of LSD. *Activ. nerv. sup.*, **5**, 215.

Hausner, M. and Dolezal, V., 1963. Group and individual psychotherapy under LSD. *Acta psychother.*, **11**, 39.

Hausner, M. and Dolezal, V., 1966. Follow-up studies in group and individual LSD psychotherapy. *Activ. nerv. sup.*, **8**, 87.

Heyder, D. W., 1963. LSD-25 in conversion reaction. *Am. J. Psychiat.*, **120**, 396.

Holzinger, R., 1964. Analytic and integrative therapy with the help of LSD-25. *J. Existential Psychiat.*, **4**, 225.

Jensen, S. E., 1962. A treatment program for alcoholics in a mental hospital. *Q. Jl. Stud. Alcohol*, **23**, 315.

Jensen, S. E. and Ramsay, R., 1963. Treatment of chronic alcoholism with lysergic acid diethylamide. *Can. psychiat. Ass. J.*, **8**, 182.

Johnsen, G., 1965. Three years' experience with the use of LSD as an aid in psychotherapy. *Acta psychiat. scand., Suppl.*, **180**, 383.

Johnson, F. G., 1961. LSD. *Canada's ment. Hlth*, **14**(3), 10.

Kafka, J. S. and Gaarder, K. R., 1964. Some effects of the therapist's LSD experience on his therapeutic work. *Am. J. Psychother.*, **18**, 236.

Kafkalidis, A., 1963. Application therapeutique de la diethylamide de l'acide d-lysergique (Delyside ou LSD-25) sur les psychonevroses. *Annls méd.-psychol.*, **121**(2), 191.

Kasahara, Y., *et al.*, 1961. LSD-25 and body image. *J. Osaka Cy med. Cent.*, **10**, 5.
Kristensen, K. K., 1963. LSD treatment in a Copenhagen department of admission. *Acta psychiat. scand., Suppl.*, **169**, 161.
Lanter, R., Weil, J. and Roth, M., 1962. Note à propos de l'utilisation diagnostique therapeutique des drogues hallucinogènes (mescaline, LSD-25). *Annls méd.-psychol.*, **120**(2), 244.
Leuner, H., 1963. Die Psycholytische Therapie: Klinische Psychotherapie mit Hilfe von LSD-25 und verwandten Substanzen. *Z. Psychother. med. Psychol.*, **13**, 57.
Leuner, H., 1964. *Zur Überlegenheit einer Durch Halluzinogene Geförderten Psychotherapie (psycholyse).* In: *Neuro-Psychopharmacology, Volume* 3. *Proceedings of the third meeting of the Collegium Internationale Neuro-Psychopharmacologicum, Munich, September* 1962. Amsterdam, Elsevier, p. 180.
Levine, J. and Ludwig, A. M., 1964. The LSD controversy. *Compreh. Psychiat.*, **6**, 314.
Levine, J. and Ludwig, A. M., 1966. The hypnodelic treatment technique. *Int. J. clin. exp. Hypnosis*, **14**, 207.
Levine, J., Ludwig, A. M. and Lyle, W. H., 1963. The controlled psychedelic state. *Am. J. Clin. Hypn.*, **6**, 163.
Livingstone, D., 1966. Some general observations on the usefulness of lysergic acid in psychiatry. *N.Z. med. J.*, **65**, 657.
Ludwig, A. M. and Levine, J., 1965. A controlled comparison of five brief treatment techniques employing LSD, hypnosis and psychotherapy. *Am. J. Psychother.*, **19**, 417.
Ludwig, A. M. and Levine, J., 1967. *Hypnodelic therapy.* In: *Current psychiatric therapies*, Vol. 7, edited by J. H. Masserman. New York and London, Grune and Stratton, p. 130.
McLean, J. R., *et al.*, 1961. The use of LSD-25 in the treatment of alcoholism and other psychiatric problems. *Q. Jl Stud. Alcohol*, **22**, 34.
MacLean, J. R. and Wilby, W. E., 1967. Treatment of alcoholism with lysergide. Comment on the article by Smart *et al.* with special reference to issues of responsibility in research reporting. *Q. Jl Stud. Alcohol*, **28**, 140.
Martin, J. A., 1964. A case of early paranoiad psychosis treated by lysergic acid diethylamide (LSD). *Acta psychother.*, **12**, 119.
Opitz, E., 1963. Die klinische Therapie seelischer Störungen mit Lysergäure. *Psychiatie Neurol. med. Psychol.*, **15**, 366.
O'Reilly, P. O. and Funk, A., 1964. LSD in chronic alcoholism. *Can. psychiat. Ass. J.*, **9**, 258.
O'Reilly, P. O. and Reich, G., 1962. Lysergic acid and the alcoholic. *Dis. nerv. Syst.*, **23**, 331.
Pos, R., 1966. LSD-25 as an adjunct to long-term psychotherapy. *Can. psychiat. Ass. J.*, **11**, 330.
Robinson, J. T., *et al.*, 1963. A controlled trial of abreaction with lysergic acid diethylamide (LSD-25). *Br. J. Psychiat.*, **109**, 46.
Rosen, I., 1963. *Clinical observations on aggression in the treatment of affective disorders with obsessions by the use of lysergic acid and intensive psychotherapy.* In: *Hallucinogenic drugs and their psychotherapeutic use. Proceedings of the Royal Medico-Psychological Association, February 1961*, edited by R. Crocket, R. A. Sandison and A. Walk. London, H. K. Lewis, p. 137.

Sandison, R. A., 1963. *Certainty and uncertainty in the LSD treatment of psychoneurosis.* In: *Hallucinogenic drugs and their psychotherapeutic use. Proceedings of the Royal Medico-Psychological Association, February 1961*, edited by R. Crocket, R. A. Sandison and A. Walk. London, H. K. Lewis, p. 33.

Sandison, R. A., 1966. Lysergic acid diethylamide. *Br. med. J.*, ii, 48.

Sarrett, M., Cheek, F. and Osmond, H., 1966. Reports of wives of alcoholics of effects of LSD-25 treatment of their husbands. *Archs gen. Psychiat.*, **14**, 171.

Savage, C., *et al.*, 1966. The effects of psychedelic (LSD) therapy on values, personality and behaviour. *Int. J. Neuropsychiat.*, **2**, 241.

Savage, C., *et al.*, 1964. LSD:therapeutic effects of the psychedelic experience. *Psychol. Rep* , **14**, 111

Savage, C. and Stolaroff, M. J., 1965. Clarifying the confusion regarding LSD-25. *J. nerv. ment. Dis.*, **140**, 218.

Savage, C., Stolaroff, M. J. and Harman, W., 1863. The psychedelic experience. *J. Neuropsychiat.*, **5**, 4.

Schoen, S. M., 1964. LSD in psychotherapy. *Am. J. Psychother.*, **18**, 35.

Sherwood, J. N., Stolaroff, M. J. and Harman, W. W., 1962. The psychedelic experience. A new concept in psychotherapy. *J. Neuropsychiat.*, **4**, 69.

Smart, R. G. and Storm, T., 1964. The efficacy of LSD in the treatment of alcoholism. *Q. Jl. Stud. Alcohol*, **25**, 333.

Smart, R. G., *et al.*, 1966. A controlled study of lysergide in the treatment of alcoholism. I. The effects on drinking behaviour. *Q. Jl. Stud. Alcohol.*, **27**, 469.

Smith, C. M., 1964. Exploratory and controlled studies of lysergide in the treatment of alcoholism. *Q. Jl. Stud. Alcohol*, **25**, 742.

Solursh, L. P., 1966. The use of LSD-25 in psychotherapy: an evaluation. *Int. J. Neuropsychiat.*, **2**, 651.

Tenebaum, B., 1961. Group therapy with LSD-25. (A preliminary report.) *Dis. nerv. Syst.*, **22**, 459.

Vanggaard, T., 1964. Indications and counter-indications for LSD treatment: observations at Powick Hospital, England. *Acta. Psychiat. Scand. Suppl.*, **180**, 427.

Whitaker, L. H., 1964. Lysergic acid diethylamide in psychotherapy. I. Clinical aspects; II. Results. *Med. J. Aust.*, i, 1; 36.

Treatment of Children

Bender, L., 1966. d-Lysergic acid in the treatment of the biological features of childhood schizophrenia. *Dis. nerv. Syst.*, **27**, 43.

Bender, L., *et al.*, 1966. *The treatment of childhood schizophrenia with LSD and UML.* In: *Biological treatment of mental illness. Proceedings of the 2nd International Conference of the Manfred Sakel Foundation, 31 October–3 November 1962*, edited by M. Rinkel. New York, Farrer, Straus and Giroux, p. 463.

Bender, L., Garetra, G. and Cobrinik, L., 1963. *LSD and UML treatment of hospitalized disturbed children.* In: *Recent advances in biological psychiatry, Volume 5*, edited by J. Wortis. New York, Plenum Press, p. 84.

Freedman, A. M., Ebin, E. V. and Wilson, E. A., 1962. Autistic schizophrenic children. An experiment in the use of D-lysergic acid diethylamide (LSD-25). *Archs gen. Psychiat.*, **6**, 203.

Rolo, A., *et al.*, 1965. Preliminary method for study of LSD with children. *Int. J. Neuropsychiat.*, **1**, 552.
Simmons, J. Q., *et al.*, 1966. Modification of autistic behaviour with LSD-25. *Am. J. Psychiat.*, **122**, 1201.

Adverse Effects

American Bar Association and the American Medical Association Joint Committee on Narcotic Drugs, 1961. *Interim and final reports: drug addiction; crime or disease?* Bloomington, Indiana University Press.
Anderson, E. W. and Rawnsley, K., 1954. Clinical studies of lysergic acid diethylamide. *Mschr. Psychiat. Neurol.*, **128**, 38.
Baker, E. F. W., 1964. The use of lysergic acid diethylamide (LSD 25) in psychotherapy. *Can. med. Ass. J.*, **91**, 1200.
Beecher, H. K., 1959. *Measurement of subjective responses: quantitative effects of drugs.* New York, Oxford University Press.
Bensoussan, P.-A., Joannides, A.-A. and Soubrier, J.-P., 1966. Note sur quelques accidents de l'usage incontrole des psycho-dysleptiques. *Annls méd.-psychol.*, **124**(2), 90.
Bewley, T. H., 1967. Adverse reactions from the illicit use of lysergide. *Br. med. J.*, iii, 28.
Blum, R., *et al.*, 1965. *Utopiates: the use and users of LSD* 25. London, Tavistock Publications.
Bolton, W. B., 1961. Schizophrenia produced by LSD 25. *Can. J. Occup. Ther.*, **28**, 55.
Boor, W. de, 1956. *Pharmakopsychologie und Psychopathologie.* Berlin, Springer.
British Medical Journal, 1966. Effects of LSD. *Br. med. J.*, i, 1495.
Calanca, A., 1963. Auto-experimentation au LSD-25 et à la psilocybine. *Schweizer Arch. Neurol. Psychiat.*, **92**, 236.
Cohen, S., 1960. Lysergic acid diethylamide: side effects and complications. *J. nerv. ment. Dis.*, **130**, 30.
Cohen, S., 1965. *Drugs of hallucination.* London, Secker.
Cohen, S., 1966. A classification of LSD complications. *Psychosomatics*, 7, 182.
Cohen, S. and Ditman, K. S., 1963. Prolonged adverse reactions to lysergic acid diethylamide. *Archs gen. Psychiat.*, **8**, 475.
Cole, J. O. and Katz, M. M., 1964. The psychotomimetic drugs: an overview. *J. Am. med. Ass.*, **187**, 758.
Comprehensive Psychiatry, 1963. Speical issue on drug addiction. *Compreh. Psychiat.*, **4**, 135.
Dally, P., 1967. Undesirable effects of marihuana. *Br. med. J.*, iii, 367.
Ditman, K. S. *Harmful aspects of the LSD experience.* Unpublished.
Faillace, L. A., 1966. Clinical use of psychotomimetic drugs. *Compreh. Psychiat.*, **7**, 13.
Fink, M., *et al.*, 1966. Prolonged adverse reactions to LSD in psychotic subjects. *Archs gen. Psychiat.*, **15**, 450.
Frosch, W. A., Robbins, E. S. and Stern, M., 1965. Untoward reactions to lysergic acid diethylamide (LSD) resulting in hospitalization. *New Engl. J. Med.*, **273**, 1235.
Garber, R. S., 1967. Discussion. *Am. J. Psychiat.*, **113**, 1209.

Geett-Jorgensen, E., *et al.*, 1965. LSD treatment. Experience gained within a three-year period. *Acta psychiat. scand., Suppl.*, **180**, 373.
Hensala, J. D., Epstein, L. J. and Blacker, K. H., 1967. LSD and psychiatric inpatients. *Archs gen. Psychiat.*, **16**, 554.
Horst, L. van der, 1961. *L'influence des facteurs spécifiques et non-spécifiques sur les effets cliniques engendrés par l'emploi de LSD.* In: *Neuro-Psychopharmacology, Volume 2. Proceedings of the second meeting of the Collegium Internationale Psychopharmacologicum, Basle, July,* 1960, edited by E. Rothlin. Amsterdam, Elsevier, p. 282.
Hyde, R. W., 1960. *Psychological and social determinants of drug action.* In: *The dynamics of psychiatric drug therapy*, edited by G. J. Sarwer-Foner. Springfield, Ill., Thomas, p. 297.
Journal of the American Medical Association, 1966. Prolonged adverse reactions to LSD. *J. Am. med. Ass.*, **198**, 658.
Keeler, M. H. and Reifler, C. B., 1967. Suicide during an LSD reaction. *Am. J. Psychiat.*, **123**, 884.
Knudsen, H., 1964. Homicide after treatment with lysergic acid diethylamide. *Acta psychiat. scand., Suppl.*, **180**, 389.
Kristensen, K. K., 1963. LSD treatment in a Copenhagen department of admission. *Acta psychiat. scand., Suppl.*, **169**, 161.
Kuramochi, H. and Takahashi, R., 1964. Psychopathology of LSD intoxication. *Archs gen. Psychiat.*, **11**, 151.
Kurland, A. A., *et al.*, 1967. Psychedelic therapy utilizing LSD in the treatment of the alcoholic patient. A preliminary report. *Am. J. Psychiat.*, **123**, 1202.
Leuner, H., 1962. *Die Experimentelle Psychose.* Berlin, Springer.
Louria, D. B., *et al.*, 1966. The dangerous drug problem. *N.Y. Med.*, **22**, 241.
Ludwig, A. M. and Levine, J., 1965. Patterns of hallucinogenic drug abuse. *J. Amer. med. Ass.*, **191**, 92.
McGlothlin, W. H. and Cohen, S., 1965. The use of hallucinogenic drugs among college students. *Am. J. Psychiat.*, **122**, 572.
McGlothlin, W. H., Cohen, S. and McGlothlin, M. S., 1966. *Long lasting effects of LSD on normals.* Santa Monica, Rand Corporation.
Miller, N. E., 1966. Some animal experiments pertinent to the problem of combining psychotherapy with drug therapy. *Compreh. Psychiat.*, **7**, 1.
New England Journal of Medicine, 1965. LSD—a dangerous drug. *New Engl. J. Med.*, **273**, 1280.
Opitz, E., 1963. Die klinische Therapie seelischer Störungen mit Lysergsäure. *Psychiatrie Neurol. med. Psychol.*, **15**, 366.
Pauk, Z. D. and Sahass, C., 1961. Some test findings associated with susceptibility to psychosis induced by lysergic acid diethylamide. *Compreh. Psychiat.*, **2**, 188.
Reynolds, H. H. and Peterson, G. K., 1966. Psychophysiological effects of a large non-experimental dose of LSD-25. *Psychol. Rep.*, **19**, 287.
Robbins, E., Frosch, W. A. and Stern, M., 1967. Further observations on untoward reactions to LSD. *Am. J. Psychiat.*, **114**, 393.
Robinson, J. T., 1960. Discussion on "An experiment with a psychiatric night hospital" by J. Bierer and I. W. Browne, *Proc. R. Soc. Med.*, **53**, 932.
Rosenthal, S. H., 1964. Persistent hallucinosis following repeated administration of hallucinogenic drugs. *Am. J. Psychiat.*, **121**, 238.

Roubicek, J. and Srnec, J., 1955. Experimental psychosa vyrolana LSD. *Cas. Lék. česk.*, **94**, 189.
Savage, C., 1957. The resolution and subsequent remobilization of resistance by LSD in psychotherapy. *J. nerv. ment. Dis.*, **125**, 434.
Seevers, M. H., 1962. Medical perspectives on habituation and addiction. *J. Am. med. Ass.*, **181**, 92.
Simmons, J. Q., *et al.*, 1966. Modification of autistic behaviour with LSD 25. *Am. J. Psychiat.*, **122**, 1201.
Spencer, A. M., 1964. Modifications in the techniques of LSD therapy. *Compreh. Psychiat.*, **5**, 232.
Szara, S., 1967. The hallucinogenic drugs—curse or blessing? *Am. J. Psychiat.*, **123**, 1513.
Terrill, J., 1962. LSD, transcendence and the new beginning: the nature of the LSD experience. *J. nerv. ment. Dis.*, **135**, 425.
Ungerleider, J. T., Fisher, D. D. and Fuller, M., 1966. The dangers of LSD. Analysis of seven months' experience in a university hospital's psychiatric service. *J. Am. med. Ass.*, **197**, 389.
Walther-Büel, H., 1953. Über Pharmakopsychiatrie. *Schweiz. med. Wschr.*, **83**, 483.
Zegans, L. S., Pollard, J. C. and Brown, D., 1967. The effects of LSD-25 on creativity and tolerance to regression. *Archs gen. Psychiat.*, **16**, 740.

Multiple Addiction

Blum, R., *et al.*, 1965. *Utopiates: the use and users of LSD*-25. London, Tavistock Publications.
Ludwig, A. M. and Levine, J., 1965. Patterns of hallucinogenic drug abuse. *J. Am. med. Ass.*, **191**, 92.
Scher, J., 1966. Patterns and profiles of addiction and drug abuse. *Archs gen. Psychiat.*, **15**, 539.
Ungerleider, J. T., Fisher, D. D. and Fuller, M., 1966. The dangers of LSD. Analysis of seven months' experience in a university hospital's psychiatric service. *J. Am. med. Ass.*, **197**, 389.

Social Factors

American Bar Association and the American Medical Association Joint Committee on Narcotic Drugs, 1961. *Interim and final reports. Drug addiction: crime or disease?* Bloomington, Indiana University Press.
Barron, F., Jarvik, M. E. and Bunnell, S., 1964. The hallucinogenic drugs. *Scient. Am.*, **210**, 29.
Cheek, F. E., 1963. Exploratory study of drugs and social interaction. *Archs gen. Psychiat.*, **9**, 566.
Cole, J. O. and Katz, M. M., 1964. The psychotomimetic drugs. *J. Am. med. Ass.*, **187**, 758.
Ditman, K. S., 1963. Psychotomimetics: pharmacodynamic and psychotherapeutic properties. *Proc. West. pharmac. Soc.*, **6**, 13.
Hausner, M. and Delezal, V., 1963. Catamnestic evaluation of psychotherapeutic results with the use of LSD. *Activ. nerv. sup.*, **5**, 215.

Hausner, M. and Dolezal, V., 1963. Group and individual psychotherapy under LSD. *Acta psychother.*, **11**, 39.

Hyde, R. W., 1960. *Psychological and social determinants of drug action.* In: *The dynamics of psychiatric drug therapy*, edited by G. J. Sarwer-Foner. Springfield, Ill., Thomas, p. 297.

Kolb, L., 1962. *Drug addiction: a medical problem.* Springfield, Ill., Thomas.

Lennard, H. L., 1964. *A proposed program of research in sociopharmacology.* In: *Psychological approaches to social behaviour*, edited by P. H. Leiderman and S. Shapiro. Stanford, Stanford University Press, p. 127.

Ludwig, A. M. and Levine, J., 1965. Patterns of hallucinogenic drug abuse. *J. Am. med. Ass.*, **191**, 92.

McGlothlin, W. H., 1964. *Hallucinogenic drugs: a perspective with special reference to peyote and cannabis.* Sanat Monica, Rand Corporation.

Scher, J., 1966. Patterns and profiles of addiction and drug abuse. *Archs gen. Psychiat.*, **15**, 539.

Schur, E. M., 1963. *Narcotic addiction in Britain and America: the impact of public policy.* London, Tavistock Publications.

Seevers, M. H., 1962. Medical perspectives on habituation and addiction. *J. Am. med. Ass.*, **181**, 92.

Slater, P. E., Morimoto, K. and Hyde, R. W., 1963. The effects of LSD upon group interaction. *Archs gen. Psychiat.*, **8**, 564.

Spencer, A. M., 1963. Permissive group therapy with lysergic acid diethylamide. *Br. J. Psychiat.*, **109**, 37.

Ungerleider, J. T., Fisher, D. D. and Fuller, M., 1966. The dangers of LSD. Analysis of seven months' experience in a university hospital's psychiatric service. *J. Am. med. Ass.*, **197**, 389.

World Health Organization, 1966. WHO Expert Committee on Dependence-Producing Drugs, fifteenth report. *Tech. Rep. Ser. Wld Hlth Org.*, **343**.

World Health Organization, 1967. Services for the prevention and treatment of dependence on alcohol and other drugs: fourteenth report of the WHO Expert Committee on Mental Health. *Tech. Rep. Ser. Wld Hlth Org.*, **363**.

CANNABIS

Abdulla, A., 1953. Cannabis indica als Volksseuche in Agypten. *Schweiz. med. Wschr.*, **83**, 541.

Adams, R., 1941–1942. Marihuana. *Harvey Lect.*, series 37, 168.

Allbutt, T. C. and Dixon, W., 1906. *Opium poisoning and other intoxications.* In: *System of medicine*, edited by T. C. Allbutt and H. D. Rolleston. London, Macmillan, vol. 2, part 1, p. 965.

Allentuck, S. and Bowman, K. M., 1942. The psychiatric aspects of marihuana intoxication. *Am. J. Psychiat.*, **99**, 248.

Ames, F., 1958. A clinical and metabolic study of acute intoxication with *cannabis sativa* and its role in the model psychoses. *J. ment. Sci*, **104**, 972.

Ammar, S. and Barek, E. M., 1961. *Study of the evolutive aspects of toxicophilia in Tunisia.* In: *Proceedings of the Third World Congress of Psychiatry, Montreal 1961.* Toronto, University Press, vol. 1, p. 407.

Andrade, O. M., 1964. The criminogenic action of cannabis and narcotics. *Bull. Narcot.*, **16**(4), 23.

Anslinger, H. J., 1943. The psychiatric aspects of marihuana intoxication. *J. Am. med. Ass.*, **121**, 212.

Asuni, T., 1964. Socio-psychiatric problems of cannabis in Nigeria. *Bull. Narcot.*, **16**(2), 17.

Baker-Bates, E. T., 1935. A case of cannabis indica intoxication. *Lancet*, i, 811.

Ball, J. C., 1967. Marihuana smoking and the onset of heroin use. *Br. J. Crim.*, **7**, 408.

Ball, J. C., Chambers, C. D. and Ball, M. J., 1967. *The association of marihuana smoking with opiate addiction in the United States.* In: *Annual Meeting of the American Sociological Association, San Francisco, California, August 28–31, 1967.*

Bartholomew, A. A. and Reynolds, W. S., 1967. Four cases of progressive drug abuse. *Med. J. Aust.*, i, 653.

Benabud, A., 1957. Psycho-pathological aspects of the cannabis situation in Morocco: statistical data for 1956. *Bull. Narcot.*, **9**(4), 1.

Beringer, K., Baeyer, W. von, and Marx, H., 1932. Zur Klinik des Haschischrausches. *Nervenarzt*, **5**, 337.

Bewley, T., 1965. Heroin and cocaine addiction. *Lancet*, i, 808.

Bewley, T., 1966. Recent changes in the pattern of drug abuse in the United Kingdom. *Bull. Narcot.*, **18**(4), 1.

Blumer, H., 1967. *The world of youthful drug use. ADD Center Project, Final Report.* Berkeley, University of California.

Boettcher, 1866. Ueber die Anwendung des indischen Hanfs in der Psychiatrie. *Berl. klin. Wschr.*, **3**, 166.

Boor, W. de, 1956. *Pharmakopsychologie und Psychopathologie.* Berlin, Springer, p. 191.

Bouquet, J., 1944. Marihuana intoxication. *J. Am. med. Ass.*, **124**, 1010.

Bouquet, J., 1950. Cannabis. *Bull. Narcot.*, **2**(4), 14.

Bouquet, J., 1951. Cannabis. *Bull. Narcot.*, **3**(1), 22.

Bozzetti, L., Goldsmith, S. and Ungerleider, J. T., 1967. The great banana hoax. *Am. J. Psychiat.*, **124**, 678.

Bromberg, W., 1934. Marihuana intoxication. A clinical study of *cannabis sativa* intoxication. *Am. J. Psychiat.*, **91**, 303.

Bromberg, W., 1939. Marihuana: a psychiatric study. *J. Am. med. Ass.*, **113**, 4.

Bromberg, W. and Rodgers, T. C., 1946. Marihuana and aggressive crime. *Am. J. Psychiat.*, **102**, 825.

Brotteaux, P., 1934. *Hachich: herbe de folie et de rêve.* Paris, Vega.

Bulletin on Narcotics, 1951. The illicit traffic in narcotics throughout the world. *Bull. Narcot.*, **3**(1), 1.

Bulletin on Narcotics, 1962. The cannabis problem: a note on the problem and the history of international action. *Bull. Narcot.*, **14**(4), 27.

Bulletin on Narcotics, 1967. Review of the 21st Session of the Commission on Narcotic Drugs. 42nd session of the Economic and Social Council of the United Nations. *Bull. Narcot.*, **19**(2), 59.

Carstairs, G. M., 1954. Daru and bhang; cultural factors in the choice of intoxicants. *Q. Jl Stud. Alcohol.* **15**, 220.

Chapple, P. A., 1966. Cannabis—a toxic and dangerous substance: a study of eighty takers. *Br. J. Addict.*, **61**, 269.

Charen, S. and Perelman, L., 1946. Personality studies of marihuana addicts. *Am. J. Psychiat.*, **102**, 674.

Chein, I., *et al.*, 1964. *Narcotics, delinquency and social policy: the road to H.* London, Tavistock Publications.

Chopra, R. N., Chopra, G. S., 1939. The present position of hemp-drug addiction in India. *Indian med. Res. Mem.*, **31**, 1.

Chopra, R. N., Chopra, G. S. and Chopra, I. C., 1942. *Cannabis sativa* in relation to mental diseases and crime in India. *Indian J. med. Res.*, **30**, 155.

Chopra, R. N. and Chopra, I. C., 1957. Treatment of drug addiction. Experience in India. *Bull. Narcot.*, **9**(4), 21.

Chopra, R. N. and Chopra, I. C., 1957. The use of cannabis drugs in India. *Bull. Narcot.*, **9**(1), 4.

Christozov, C., 1965. L'aspect marocain de l'intoxication cannabique d'après des études faites dans les conditions d'un hôpital psychiatrique de malades chroniques. *Maroc méd.*, **44**, 630; 866.

Clerambault, de, 1920. Discussion de l'article de L. Livet intitulé: Les fumeurs de mariguana. *Annls. méd.-psychol.*, **12** (10th series), 267.

Clouston, T., 1896. The Cairo Asylum: Dr. Warnock on hashish insanity. *J. ment. Sci.*, **42**, 790.

Coles, W. H., 1935. Cannabis indica. *Lancet*, i, 904.

Conos, B., 1925. Trois cas de cannabisme avec psychose consécutive. *Bull. Soc. Path. exot.*, **18**, 788.

Curtis, H. C. and Wolfe, J. R., 1939. Psychosis following the use of marijuana with report of cases. *J. Kans. med. Soc.*, **40**, 515.

Dally, P., 1967. Undesirable effects of marihuana. *Br. med .J.*, iii, 367.

Dealy, J., 1944. Les mésaventures d'un hachischin. *Presse méd.*, **52**, 321.

Deschamps, A., 1932. *Ether, cocaine, haschich, petoyl et démence précoce.* Paris, Vega.

Dhunjibhoy, J. E., 1930. A brief résumé of the types of insanity commonly met with in India, with a full description on "Indian hemp insanity" peculiar to the country. *J. ment. Sci.*, **76**, 254.

Drapkin, I. and Landau, S. F., 1966. Drug offenders in Israel: a survey. *Br. J. Crim.*, **6**, 376.

Drewry, P. H., 1936. Some psychiatric aspects of marihuana intoxication. *Psychiat. Q.*, **10**, 232.

Durand, V. J., 1955. Encyclopédie Médico-Chirurgicale, 37380, A20, p. 3. Edited by E. Y. Henri. Paris [Group de l'Evolution Psychiatrique].

Dwarakanath, S. C., 1965. Use of opium and cannabis in the traditional systems of medicine in India. *Bull. Narcot.*, **17**(1), 15.

Eddy, N. B., *et al.*, 1965. Drug dependence: its significance and characteristics. *Bull. Wld Hlth Org.*, **32**, 721.

Elkes, J., 1963. The dysleptics: note on a no-man's land. *Compreh. Psychiat.*, **4**, 195.

Emerick, C. A., 1962. *The control program of the U.S. Bureau of Customs.* In: *Proceedings of the White House Conference on Narcotic and Drug Abuse, Washington, D.C.*, 1962. Washington, Government Printing Office, p. 28.

Ewens, G. F. W., 1908. *Insanity following the use of Indian hemp.* In: *Insanity in India.* Calcutta, Thacker, Spink, p. 129.

Fontoynont, M., 1938. A propos de l'intoxication des Malgaches per le "rongony" (chanvre). *Bull. Soc. Path. exot.*, **31**, 446.
Fraenkel, F. and Joel, E., 1927. Beitrag zu einer experimentallen Psychopathologie. Der Haschischrausch. *Z. ges. Neurol. Psychiat.*, **111**, 84.
Fraser, J. D., 1949. Withdrawal symptoms in Cannabis indica addicts. *Lancet*, ii, 747.
Freedman, H. L. and Rockmore, M. J., 1946. Marihuana: a factor in personality evaluation and army maladjustment. *J. clin. Psychopath.*, **7**, 675.
Freusberg, 1877/78. Ueber die Sinnestäuschungen im Hanfrausch. *Allg. Z. Psychiat.*, **34**, 216.
Gaskill, H. S., 1945. Marihuana, an intoxicant. *Am. J. Psychiat.*, **102**, 202.
Ginsburg, D. and Kaufman, J. L., 1955. Problems of drug addiction in Israel. *Bull. Narcot.*, **7**(1), 15.
Gokay, F. K., 1937. Durch Missbrauch von Heroin und Haschisch entstehende Geisteskrankheiten in der Turkei. *Z. ges. Neurol. Psychiat.*, **158**, 428.
Gomila, F. R., 1938. *Present status of the marihuana vice in the United States.* In: *Marihuana: America's new drug problem*, by R. D. Walton, Philadelphia, Lippincott, p. 27.
Halleck, S. L., 1967. Psychiatric treatment of the alienated college student. *Am. J. Psychiat.*, **124**, 642.
Haneveld, G. T., 1959. Brieven uit den Vreemde. *Ned. Tijdschr. Geneesk*, **103**(1), 686.
Harms, E., editor, 1965. *Drug addiction in youth.* London, Pergamon.
Hesnard, A., 1912. Note sur les fumeurs de chanvre en orient. *Encéphale*, **2**, 40.
Hoffman, H. R., *et al.*, 1962. Teen-age drug addicts arraigned in the narcotic court of Chicago. *J. Am. med. Ass.*, **149**, 655.
Igert, G., 1955. Milieu culturel marocain et névroses. *Maroc. méd.*, **34**, 648.
Indian Hemp Drugs Commission, 1894. Report. Simla and Calcutta, Government Central Printing Office.
Interdepartmental Committee on Narcotics, 1956. Report to the President of the United States. *Bull. Narcot.*, **8**(2), 4.
Ireland, T., 1893. Insanity from the abuse of Indian hemp. *Alien. Neurol.*, **14**, 622.
Kabelik, J., Krejci, Z. and Santavy, F., 1960. Cannabis as a medicament. *Bull. Narcot.*, **12**(3), 5.
Kant, F., 1930. Ueber Reaktionsformen im Giftrausch, mit einem Beitrag zum Halluzinationsproblem. *Arch. Psychiat. NervKrankh.*, **91**, 694.
Kant, F. and Krapf, E., 1928. Ueber Selbstversuche mit Haschisch. *Arch. exp. Path. Pharmak.*, **129**, 319.
Keeler, M. H. and Reifler, C. B., 1967. Grand mal convulsions subsequent to marihuana use. *Dus. nerv. Syst.*, **28**, 474.
Keeler, M. H., 1967. Adverse reaction to marihuana. *Am. J. Psychiat.*, **124**, 674.
Koppikar, G. S., 1948. Drug addiction in Bombay: opium, bhang, ganja. *Indian J. med. Sci.*, **2**, 131.
Lambo, T. A., 1965. Medical and social problems of drug addiction in West Africa. *Bull. Narcot.*, **17**(1), 3.
Lancet, 1890. Toxic effects of cannabis indica. *Lancet*, i, 621.
Lasagna, L., von Felsinger, J. M. and Beecher, H. K., 1955. Drug-induced mood changes in man. *J. Am. med. Ass.*, **157**, 1006; 1113.

Lindemann, E. and Malamud, W., 1934. Experimental analysis of the psychopathological effects of intoxicating drugs. *Am. J. Psychiat.*, **90**, 853.
Lindesmith, A. R., 1965. *The addict and the law.* Bloomington, Indiana University Press.
Livet, L., 1920. Les fumeurs de mariguana. *Annls. méd.-psychol.*, **12** (19th series), 257.
Lucena, J., 1939. Maconhismo e alucinações. *Neurobiologia*, **2**, 110.
Lucena, J., 1961. *La symptomatologie du cannabisme.* In: *Proceedings of the Third World Congress of Psychiatry, Montreal 1961.* Toronto, University Press, vol. 1, p. 401.
Lucena, J., Ataide, L. and Coelho, P., 1949. Maconhismo cronico e psicoses. *Neurobiologia*, **12**, 235.
Marcovitz, E., 1945. Marihuana problems. *J. Am. med. Ass.*, **129**, 378.
Marcovitz, E. and Myers, H. J., 1944. Marihuana addiction in the army. *War. Med.*, (*Chicago*), **6**, 382.
Marie, A., 1907. Note sur la folie haschichique (à propos de quelques Arabes alienés par le haschich). *Nouv. Iconogr. Salpet.*, **20**, 252.
Meggendorfer, F., 1928. *Intoxikations-psychosen.* In: *Handbuch der Geisteskrankheiten*, Vol. 7. Berlin, Bumke, p. 353.
Meunier, R., 1909. *Hachich.* In: *Dictionnaire de Physiologie* [Ch. Richet]. Paris, Alcan, p. 188.
Moreau, J., 1857. Lypémanie avec stupeur: tendence à la démence, traitement par l'extrait (principe résineux) de *cannabis indica*: guérison. *Gaz. Hop. civ. milit., Paris*, **30**, 391.
Munch, J. C., 1966. Marihuana and crime. *Bull. Narcot.*, **18**(2), 15.
Murphy, H. B. M., 1963. The cannabis habit. *Bull. Narcot.*, **15**(1), 15.
New York Academy of Medicine, 1955. Report on drug addiction, I. *Bull. N.Y. Acad. Med.*, **31**, 592.
New York Academy of Medicine, 1963. Report on drug addiction, II. *Bull. N.Y. Acad. Med.*, **39**, 417.
New York, Mayor's Committee on Marihuana, 1944. *The marihuana problem in the city of New York: sociological, medical, psychological and pharmacological studies.* Lancaster, Pa., Cattell Press.
Nyswander, M. E., 1956. *The drug addict as a patient.* New York, Grune and Stratton.
O'Shaughnessy, W. B., 1842. On the preparations of the Indian hemp, or gunjah; their effects on the animal system in health and their utility in the treatment of tetanus and other convulsive diseases. *Trans. Med. and Physical. Soc. Calcutta*, **8**(2), 421.
Parreiras, D., 1965. Census of drug addicts in Brazil—the incidence and nature of drug addiction. *Bull. Narcot.*, **17**(1), 21.
Paulus, I. and Williams, H. R., 1966. Marihuana and young adults. *Addictions*, **13**, 26.
Pearlman, S., 1967. Drug experience in an urban college population. *Am. J. Orthopsychiat.*, **37**, 297.
Peebles, A. S. M. and Mann, H. V., 1914. Ganja as a cause of insanity and crime in Bengal. *Indian med. Gaz.*, **49**, 395.
Perrussel, G., 1925. Notes préliminaires sur la psychopathologie des fumeurs de chanvre en Tunisie. *Archs. Insts. Pasteur, Afr. N.*, **14**, 434.

Pinho, R. de, *et al.*, 1962. Contribuiçaõ a mesa redonda sôbre "problemas socio-psicológicos do maconhismo", V Congresso da Sociedade de Neurologia, Psiquiatria e Higiene Mental do Brasil. *Neurobiologia*, **25**(3), 9.

Porot, A., 1941. La lutte contre l'opium et les stupéfiants sur le plan international, en ces dernières annees. *Annls. méd.-psychol.*, **99**(i), 97.

Porot, A., 1942. Le cannabisme (haschich, kif, chira, marihuana). *Annls. méd.-psychol.*, **100**(i), 1.

Rech, M., 1848. Des effets du hachisch sur l'homme jouissant de sa raison et sur l'aliéné. *Annls. méd.-psychol.*, **12**, 1.

Reed, C. F. and Witt, P. N., 1965. Factors contributing to unexpected reactions in two human drug-placebo experiments. *Confinia psychiat.*, **8**, 57.

Reichard, J. D., 1944. The marihuana problem. *J. Am. med. Ass.*, **125**, 594.

Reichard, J. D., 1947. Addiction: some theroretical considerations as to its nature, cause, prevention and treatment. *Am. J. Psychiat.*, **103**, 721.

Reko, V. A., 1936. *Magische Gifte: Rausch- und Betäubungsmittel der neuen Welt.* Stuttgart, Enke, p. 61.

Reynolds, J. R., 1890. On the therapeutic uses and toxic effects of cannabis indica. *Lancet*, i, 637.

Rolls, E. J. and Stafford-Clark, D., 1954. Depersonalization treated by cannabis indica and psychotherapy. *Guy's Hosp. Rep.*, **103**, 330.

Rosenbloom, J. R., 1959. Notes on Jewish drug addicts. *Psychol. Rep.*, **5**, 769.

Schur, E. M., 1963. *Narcotic addiction in Britain and America.* London, Tavistock Publications.

Scouras, Ph., 1939. Le syndrome catatonique des psychoses cannabiques aigues. *Encéphale*, **34**, 78.

Shaw, W. S. J., 1923. Cannabis indica: a dangerous drug. *Br. med. J.*, ii, 586.

Silberman, M., 1967. *Aspects of drug addiction.* London, Royal London Prisoners' Aid Society.

Siler, J. F., 1933. Marijuana smoking in Panama. *Milit. Surg.*, **73**, 269.

Sington, D., editor, 1965. *Psychosocial aspects of drug-taking. Proceedings of a one-day conference held at University College, London, 25th Sept.*, 1964. Oxford, Pergamon.

Skliar, N. and Iwanow, A., 1932. Ueber den Anascha-Rausch. *Allg. Z. Psychiat.*, **98**, 300.

Skliar, N., 1934. Ueber Anascha Psychosen. *Allg. Z. Psychiat.*, **102**, 304.

Sonnenreich, C. and Goes, J. P., 1962. Maconha e disturbios psiquico. *Neurobiologia*, **25**, 69.

Soueif, M. I., 1967. Hashish consumption in Egypt, with special reference to psychosocial aspects. *Bull. Narcot.*, **19**(2), 1.

Stringaris, M. G., 1933. Zur Klinik der Haschischpsychosen (Nach Studein in Griechenland). *Arch. Psychiat.*, **100**, 522.

Todd, A. R., 1943. The hemp drugs. *Endeavour*, **2**, 69.

Tramer, L. and Bentovim, L., 1961. Clinical psychological study on Eastern drug addicts. *Confinia psychiat.*, **4**, 194.

Tull-Walsh, J. H., 1894. Hemp drugs and insanity. *J. ment. Sci.*, **40**, 21.

United Nations, Commission on Narcotic Drugs, 1967. *Review of illicit traffic 1966–1967.* (E/CN.7/506) Geneva, United Nations.

United Nations, Commission on Narcotic Drugs, 1966. *Abuse of drugs: drug addiction, in particular its economic and social aspects.* (E/CN.7/496). Geneva, United Nations.

United States. President's Commission on Law Enforcement and Administration of Justice, 1967. *Challenge of crime in a free society: a report.* Washington, Government Printing Office, p. 211.

Vaille, C. and Stern, G., 1954. Drug addiction: medical and social aspects in France. *Bull. Narcot.*, **6**(2), 1.

Vierth, G., 1967. Psychopathologische Syndrome nach Haschisch-Genuss. Beobachtungen asu Marokko. *Münch. med. Wschr.*, **109**, 522.

Vogel, V. H., Isbell, H. and Chapman, K. W., 1948. Present status of narcotic addiction with particular reference to medical indications and comparative addiction liability of the newer and older analgesic drugs. *J. Am. med. Ass.*, **138**, 1019.

Vogel, V. H. and Isbell, H., 1950. Medical aspects of addiction to analgesic drugs. *Bull. Narcot.*, **2**(4), 31.

Walton, R. P., 1945. Marijuana problems. *J. Am. med. Ass.*, **128**, 383.

Walton, R. P., 1938. *Marijuana: America's new drug problem.* Philadelphia, Lippincott.

Warnock, J., 1903. Insanity from hasheesh. *J. ment. Sci.*, **49**, 96.

Watt, J. M. and Breyer-Brandwijk, M. G., 1936. The forensic and sociological aspects of the dagga problem in South Africa. *S. Afr. med. J.*, **10**, 573.

Wolff, P. O., 1949. *Marihuana in Latin America: the threat it constitutes.* Washington, Linacre Press.

Wolstenholm, G. E. W. and Knight, J., editors, 1965. *Hashish: its chemistry and pharmacology.* (Ciba Foundation Study Group No. 21.) London, Churchill.

World Health Organization, 1967. Services for the prevention and treatment of dependence on alcohol and other drugs: fourteenth report of the WHO Expert Committee on Mental Health. *Tech. Rep. Ser. Wld Hlth Org.*, **363**.

Yawger, N. S., 1938. Marihuana: our new addiction. *Am. J. med. Sci.*, **195**, 351.

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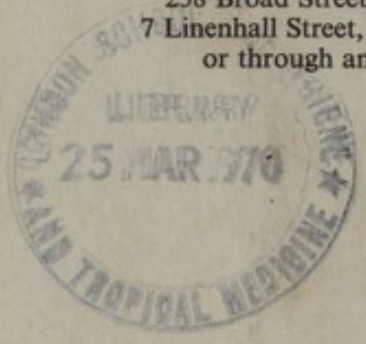

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