Psychoses Associated with Drug Use

Malcolm B. Bowers, Jr. and Daniel X. Freedman

American Handbook of Psychiatry

Psychoses Associated with Drug Use

Malcolm B. Bowers, Jr. and Daniel X. Freedman

e-Book 2015 International Psychotherapy Institute

From *American Handbook of Psychiatry: Volume 4* edited by Silvano Arietti

Table of Contents

Psychoses Associated with Drug Use

Introduction

This chapter deals with the genesis of psychotic behavior in which intake of a pharmacologic compound plays a significant role. As used here, *psychosis* refers to an experience of self and external world, which, for a significantly prolonged period, is at marked variance with generally accepted notions of reality and which is not under individual control. Psychotic behavior may become manifest at a variety of stages in the course of drug use: during acute or chronic drug ingestion, during drug withdrawal, or at varying intervals following drug use. In the latter instance the contribution of the drug to the genesis of the psychotic behavior is often hard to assess.

The phenomena of drug-induced altered states of consciousness which involve marked but usually temporary distortion in self-image, feeling states, and perception of external reality, remind psychopathologists that one component of many major psychiatric syndromes are just such alterations in consciousness. In the naturally occurring psychotic reaction such states of mind may be long lasting, recurrent, evoked in response to individually perceived experience, and with time variously assimilated or rejected by the individual. The fact that the same or similar statements can currently be made about many drug-related states encountered clinically indicates just how

instructive the drug model has become.

Psychotic behavior is more likely to occur in a higher dose range and following prolonged use of a given compound with psychotogenic potential. When such behavior occurs at a lower dose, is not associated with delirium, and extends beyond the known period of drug action, one suspects the presence of other factors which may have predisposed the individual to such a response. Such factors may include a broad range of conscious and unconscious situational or maturational stresses—psychosocial stresses, which might threaten the coping capacities of the individual. Such stresses may have been involved in the original motivation to use the drug in question.

A classification of syndromes produced by drugs with psychotogenic potential with regard to the presence or absence of delirium, the contribution of psychosocial stress, and relative similarity to naturally occurring states is somewhat arbitrary. However, the classification proposed by Brawley and Duffield in their review of hallucinogenic drugs, has some utility for the purposes of this survey.

Many active drugs, administered long enough and in sufficient quantity, produce psychotic behavior as part of a more extensive spectrum of general metabolic, neurologic, or toxic effects. The psychic syndrome thus produced is usually associated with some evidence of intellectual impairment, such as

restricted consciousness, memory loss, or disorientation. Thus many of the symptoms of acute toxic psychosis are those of acute brain syndrome. We recognize in reality that a continuum exists between compounds which produce psychotic phenomena in a clouded as opposed to a clear sensorium. With some exceptions, compounds which produce primarily acute brain syndrome or neurotoxic effects usually do not produce psychotic syndromes akin to the naturally occurring psychoses nor do their effects usually persist after the drug has been withdrawn, unless damage to the central nervous system has occurred. Brawley and Duffield refer to these compounds as "poisons," though actually they represent a heterogeneous group.

A group of drugs with anticholinergic properties tends to produce delirium without extensive toxic effects on other systems. This clinical syndrome is characterized by restricted consciousness; disorientation to time, place, and person; impairment in recent memory; visual hallucinations; and some degree of retrograde amnesia. Yet a third group of drugs—the

Psychotomimetic hallucinogens—can produce acute psychotic states without markedly clouding consciousness or producing other signs of intellectual impairment. These states resemble more closely some manifestations of the naturally occurring psychoses but are usually approximately limited in time by the duration of drug action. However, in some instances, use of these compounds is coincidental with or effective in

precipitating extended psychotic states in some vulnerable individuals. Neither the nature of such vulnerability nor the role of drug effects interacting with such factors has been defined.

Psychotogenic Drugs with Generalized Metabolic or Toxic Effects

Almost any potent pharmaceutical agent can potentially be placed in this category. Drugs which mimic or alter hormonal systems seem particularly likely to produce psychotic reactions in some individuals. High doses of adrenal steroids and ACTH are noted for their potential psychotomimetic effects. Although the literature is not in complete accord, many psychotic reactions produced by these agents have not been associated with delirium and have resembled so-called schizoaffective reactions. There is no mandatory mood change contingent upon hormonal excesses or deficiencies but euphoria as a component of mood change with steroid medication is not uncommon; perceptual changes with reference to the body and the environment can accompany any of these mood changes. We are aware of a few instances of self-medication with drugs such as prednisone in order to enhance affect. Psychosocial factors contributory to psychotomimetic reactions may be important when the steroid treatment is administered for life-threatening illness (for instance, systemic *lupus erythematosus*) or produces gross weight gain and change in facial appearance. In the case of systemic *lupus erythematosus* vascular changes in the central nervous system may be contributory to behavioral change. In the treatment of thyroid dysfunction a variety of behavioral reactions may ensue contingent upon thyroid status, treatment agent, or change in psychological organization. Psychotic reactions have been reported in association with the

administration or withdrawal of oral contraceptive preparations.

Although little used today, bromide preparations used to be a major cause of psychotic reactions. Usually such psychoses were associated with significant disorientation, but Levin has described a “bromide schizophrenia” which he feels differs from bromide delirium in that clouding of consciousness was not a symptom in the former condition, and differential diagnosis on admission for such disorders presented a challenge to the astute clinician. The variety of psychological states which bromides can produce are not familiar to many clinicians today, but Levin’s studies document an array of syndromes more prominent when bromides were more readily available in proprietary sedative preparations. Replacement of retained bromide with saline was a useful therapy. Bromides are still present in a few over-the-counter preparations, but they have largely been replaced by belladonna alkaloids.

Acute inhalation of a variety of volatile organic solvents can result in unusual states of consciousness. These agents vary in their toxicity. Gasoline, toluene, ethyl acetate, and trichlorethylene are among the compounds which can produce “inhalation psychoses.” Some individuals may develop habituation to such practices and polyneuropathy has been reported. Most of these compounds are anesthetics and acute inhalation in poorly ventilated surroundings can result in unconsciousness and death from suffocation (glue

sniffing) or a primary cardiac toxicity from fluorinated hydrocarbons in aerosols (Freon). The acute brain syndrome produced by inhalation of organic solvents is usually attended by clouding of consciousness and terminated soon after the offending compound has been removed.

Unique psychopharmacological properties have been described for the anesthetic phencyclidine (Semyl) now primarily used in veterinary medicine. Extensively studied by Domino, Luby, and their colleagues, this compound in subanesthetic doses produces a unique picture of dissociation of consciousness akin to sensory isolation in which the individual may experience a variety of distortions in body image. Although clouding of consciousness may be present, cognitive and body image changes produced by phencyclidine have reminded some investigators of the primary clinical symptoms of schizophrenia. This compound has recently been found extensively on the illicit drug market (known as PCP) and often is an unexpected adulterant of material sold as LSD or mescaline.

Use of the antimalarial drug atabrine was associated with psychotic reactions during World War II. Most of these cases were apparently characterized by disorientation but several were quite prolonged. Some correlation with accumulated drug or metabolite was apparent and paranoid features were prominent, presenting problems for differential diagnosis.

Psychosis may occur as part of a syndrome of withdrawal from drugs which produce tissue dependence such as the major narcotics and sedative antianxiety drugs, including ethyl alcohol, barbiturates, meprobamate, and the benzodiazepines. Withdrawal from sedative compounds generally produces neurological symptoms such as tremor and convulsions but, as classic studies have shown, hallucinations and delirium can be a prominent aspect of the syndrome of sedative withdrawal. As is generally known, the onset of all or part of this syndrome may be delayed following withdrawal of sedative compounds. In part, this phenomenon is related to a long half-life of certain drugs such as meprobamate or chlordiazepoxide. The classic state of sedative withdrawal (delirium tremens) which occurs following ethyl alcohol is not considered a specific indication for antipsychotic phenothiazine drugs. In fact under certain conditions such drugs may be contraindicated as they are in belladonna delirium (central anticholinergic syndrome).

Deliriants-Atropinelike Drugs

Many drugs used in medical practice have atropinelike properties. In general these compounds are quite potent and may produce psychotic effects at doses of a few milligrams. The psychosis thus produced is the typical "belladonna delirium" or central anticholinergic syndrome characterized by disorientation, dry skin, mydriasis, tachycardia, visual hallucinations, amnesia, and slowing of the electroencephalogram. This clinical picture usually subsides within twenty-four hours after the offending drug or drug combination has been discontinued. Older individuals with chronic brain syndrome or other factors predisposing to delirium are usually susceptible to psychotic reactions produced by these compounds. This syndrome can be specifically reversed by the administration of physostigmine, but conservative management is usually sufficient once the atropinelike drug has been withdrawn. Phenothiazines (which possess anticholinergic properties) have been reported to exacerbate atropinelike psychosis so that differential diagnosis of this state from psychosis related to amphetamine or LSD-like drugs is essential, for in the latter cases phenothiazines and sedative antianxiety compounds, respectively, are usually helpful. The atropinelike psychosis frequently emerges in clinical psychiatric practice when a patient is receiving a combination of drugs which have anticholinergic properties such as phenothiazines, tricyclic antidepressants, and anti-Parkinsonian compounds. It is generally believed that these psychotic reactions are related

to the interruption of function in the central cholinergic neuronal systems. However, it is unclear why higher psychic, function is affected early in the dose-response spectrum of the centrally acting anticholinergics, whereas anticholinesterase compounds tend to produce more widespread and life-endangering neurotoxic effects and a different pattern of altered psychic function with some similarities to depressive states.

Psychotomimetic Drugs

Amphetaminelike Drugs

Compounds with actions similar to amphetamine (methamphetamine, cocaine, methylphenidate, phenmetrazine, and diethylproprion) may produce psychotic reactions without marked clouding of consciousness. Three years after the first use of amphetamine in the treatment of narcolepsy, psychotic reactions were reported. These authors also speculated on the possible vulnerability of persons with psychopathic traits to such drug use and reactions. In more recent years, the use of amphetaminelike drugs for appetite suppression and psychomotor stimulation has led to periodic occurrence of such reactions.

At higher doses and with continuing use amphetaminelike drugs reliably produce psychotic symptoms which often cannot be distinguished from those of naturally-occurring paranoid psychoses. It has been recently shown under certain experimental conditions that these compounds regularly produce a syndrome of psychotic suspiciousness and ideas of reference. These clinical studies, in which amphetamine has been repeatedly administered to volunteer subjects so a relatively large cumulative intake is achieved over a few days, suggest that virtually all subjects will eventually become psychotic on such a regimen. Since the subjects have been amphetamine users, the factor of prior state (including personality) must be

considered as a component in the response. Many investigators consider this high-dose amphetamine reaction the closest experimental analogue of the naturally-occurring psychoses. Bell, however, has recounted administration of higher doses of intravenous methamphetamine in amphetamine addicts. He frequently observed very prompt onset of symptoms. These, however, are initially changes in perception, illusions, tension, and difficulty in locating the source and meaning of such changes. Paranoid interpretations followed later, as did the more typical ideas of reference and delusions. He observes this pattern in one group of cases encountered clinically whose symptoms eventually subsided while another group with auditory hallucinations had persisting symptoms. These changes are not unlike the sequence of events observed with the psychotomimetic indoles (LSD, psilocybin, DMT [N,N1-dimethyltryptamine]) and phenylethylamines (mescaline). Indeed sharp observation and reconstruction of the early onset of amphetamine psychoses indicate sensitivity to lights and reflections; perceptual changes precede and are later "explained," resulting in the more characteristic clinical signs (paranoid delusions) by which the amphetamine reaction is generally compared to acute schizophrenia.

The fact that clinically effective antipsychotic compounds can antagonize the effects of amphetamine, and the differential effects of stereoisomers of this drug upon catecholamine systems strengthens the argument that the effects of amphetamine may be a clue to neuronal

mechanisms involved in some manifestations of the naturally-occurring psychoses. This subject has recently been reviewed by Snyder. Many similarities exist between experimental amphetamine intoxication in animals and the clinical behaviors which are encountered, notably stereotypy. Ellinwood and his coworkers have analyzed amphetamine intoxication in several species from behavioral, histochemical, neurophysiological, and neuropathological points of view.

Even at low doses amphetaminelike compounds may occasionally produce psychotic states and such psychoses may be prolonged, resembling naturally-occurring paranoid psychosis. Under these circumstances one may speak of a drug-precipitated or drug-induced psychosis, the assumption being that amphetamine ingestion facilitated some process already moving the individual in the direction of a psychotic state. The following case illustrates the way in which amphetaminelike drugs may act synergistically to exacerbate a nascent psychotic state.

A twenty year-old woman, socially undeveloped and insecure, began her first job in a clothing store following graduation from high school. She became self-conscious when male employees made sexually provocative remarks. Soon she began to believe that other employees were saying and doing things designed to tell her that she should “grow up and masturbate.” In this context she took one 5-milligram amphetamine tablet furnished by her brother. Her

thought processes accelerated greatly, and her self-experience rapidly became severely disorganized. In a few days she was admitted to a hospital with a diagnosis of acute schizophrenia. Four months of hospitalization and phenothiazine drugs were required to bring her psychotic state under control.

It has become common practice for psychiatrists to assert that individuals who suffer prolonged psychotic reactions following low doses of amphetamine, cannabis, or LSD-like drugs were "already schizophrenic" or "latent schizophrenics." This judgment is always made retrospectively and involves some assumptions about schizophrenia which are unproven, including the idea that the preschizophrenic state can be characterized and recognized. The implication in these instances that the drugs play a relatively unimportant role in the emergence and perpetuation of psychotic symptoms may be unwarranted.

Several interesting clinical interactions of amphetamine with schizophrenia add to the puzzles as to underlying mediating systems that might be common to drugs and naturally occurring syndromes. There are some instances of amphetamine psychoses which persist and can be explained very much as persisting hallucinosis as explained in alcoholism, i.e., the evocation of or unmasking of some prior psychotic disorder or symptom. When amphetamine was given to catatonic schizophrenics, they showed a

"paradoxical" reaction of drowsiness and unresponsiveness (also seen in delirium tremens), whereas amytal "awoke" the catatonic patients and seemed to relax them sufficiently to relate with some degree of normalcy for a brief period. When methylphenidate was given to persons recovering from acute schizophrenic episodes, the schizophrenic behavior was observed to recur, but when sufficient time for remission had taken place, the methylphenidate no longer evoked schizophrenic symptomatology. The utility of these various cross comparisons probably lies in the spur they give to empirical research both at the clinical pharmacological and observational levels and in animal brain-behavior research: it is as if one is constantly narrowing down a focus upon the differentiating mechanisms.

Amphetaminelike drugs have recently been extensively used by the illicit drug community. High doses are frequently administered orally or intravenously. In such a setting, brief psychotic reactions are common and often accompanied by dangerously aggressive behavior. Such amphetamine abuse can also be associated with consequences which are life-threatening to the user, including subarachnoid hemorrhage and the usual serious medical complications of intravenous drug abuse.

Amphetaminelike compounds combined with other drugs are frequently employed as bronchodilators for the treatment of asthma and other upper respiratory syndromes. Psychotic reactions have been reported

following the use of such preparations, but so too has the phenomenon of alternating psychosis and asthma in a few individuals.

LSD-like Drugs

The discovery of d-lysergic acid diethylamide (LSD) by Hoffman gave the world its most potent known mind-altering substance. Quantities less than 1 mg. of this compound produce a syndrome which may resemble certain stages in the naturally-occurring psychoses. Other related compounds such as psilocybin and dimethyltryptamine produce similar acute behavioral responses. This reaction is characterized by dramatic visual illusions and by a unique destructuring of the usual psychic defenses. Giarman and Freedman's description aptly characterizes this altered state of consciousness:

> Psychotomimetic drugs such as d-lysergic acid diethylamide . . . reliably and consistently produce periods of altered perception and experience without clouded consciousness or marked physiological changes; mental processes that are usually dormant and transient during wakefulness become "locked" into a persistent state. The usual boundaries which structure thought and perception become fluid; awareness becomes vivid while control over input is markedly diminished; customary inputs and modes of thought and perception become novel, illusory, and portentous; and with the loss of customary controlling anchors, dependence on the surroundings, on prior expectations, or on a mystique for structure and support is enhanced. Psychiatrists recognize these primary changes as a background state out of which a number of secondary psychological states can ensue, depending on motive, capacity and circumstance. This is reflected in the terminology that has grown around these drugs; if symptoms ensue, the term psychotomimetic or psychodysleptic is used; and if mystical experience, religious conversion, or a therapeutic change in

> behavior is stressed, the term psychedelic or mind "manifesting" has been applied.
>
> The drugs and clinical states set up a "search for synthesis," and the motives and capacities of subjects and patients to achieve this are obviously of importance if one is to assess outcomes and compare and contrast these states, [p. 2]

The following example of LSD-induced altered state of consciousness exemplifies the kind of experiential destructuring which may attend the use of this and similar compounds. This letter was written by a young college student during the ten hours of an LSD experience. He recovered completely at the end of this period and did not, in retrospect, regard this drug experience as a "bad trip."

Hi again Marilyn. I think that you hurt me and I haven't had the honesty to admit it so there I have admitted it and you can be happy. ... It is late and I'm getting very high with a gross and stupidly terrible idea. I must admit Marilyn, yes, that you are so much like my mother. It's like Mom when she used to punish me, she used to hit me and I think you will hit your children a lot like my mother. Yes, in your admonishing role you are like my mother, with the same kind of disapproval of my behavior it's the same feeling that I used to get when my mother disapproved of my doing something that I get now when Marilyn says I'm irresponsible. It's the same feeling I mean that when I was young I had a kind of feeling of guilt, remorse, anger, and shame—all of the normal little child's feelings. I have the same kind of feeling now

when Marilyn my mother admonishes and reprimands me for my irresponsibility and I fear that when she gives me the same feeling I used to get from my mother, then she couldn't be good for my children and my children are very important. ... I think I have finally figured it out! I'm afraid that I am going to die. If I die and I am not a Christian I will go to hell. God, am I afraid to die! I might commit suicide. My papers are due—my papers are due. . . . Why am I so afraid to lose Marilyn. There is a sense in which my fear of going insane is linked with losing her. ... I am only now very tired, a bit depressed about my papers and sorry about Marilyn so I am really alright. ... At least I have enough sense to go to bed now. I fear being crazy and admitting it to myself because then I might commit suicide like my brother. I'm going to bed. If Bill goes to the University Health he might be right and if they found out that I'm crazy I might really be crazy and if I were crazy I might commit suicide. I'm afraid everything is closing in on me, troopers and everything. I'm so tired! I'm going to bed—good night Marilyn.

This excerpt is not presented as a typical LSD experience, but rather as an experiential account suggesting the manner in which this kind of altered consciousness may reactivate certain painful intrapsychic issues and heighten the experience of conflict at certain critical developmental periods. Such an interaction between drug-induced state and intrapsychic conflict and defense may be involved in many "bad trips" or extended psychotic states related to drug use. Bridger's ideas concerning the interaction of stress and

psychotomimetic drug effect seem relevant in this context. He notes that animal experiments suggest that psychotomimetic drugs facilitate the association of a conditioned and an unconditioned stimulus so long as the animal is still under the stress of a learning paradigm where an aversive unconditioned stimulus is being used. Bridger concludes that such drugs facilitate the intrapsychic merging of symbol and the object symbolized.

We have noted that conflicts which are depicted in the phenomenology of psychotomimetic drug-induced states can be understood as genuine conflictual issues for the individual which were under control prior to the drug-induced state. The drug experience appeared to have breached an intrapsychic buffer zone between certain kinds of current experience and internal "symbols" of vulnerability, similar to the way an antigen-antibody response might be facilitated. A similar mechanism has been called "catathymic" and proposed by Faergeman as operative in "psychogenic psychoses". The ability of the individual to control, tolerate, or modulate this "anamnestic response" would be expected to vary, as it does in drug-induced states.

That stress or conflict occurring *during* a psychotomimetic episode can lead to further dyscontrol over the content, intensity, and quality of subjective experience has been noted by the adherents of the Peyote ceremonies, "lay pharmacologists" using these drugs, and medical scientists. Blacker

speculated that avoidance of aversive stimuli, learned in the drug state (in which the least stressful adaptation is to cease vigilant reaction and "go with" the experience) may characterize some of the passivity and amotivational behavior of chronic drug users. The loss of perceptual constancies, of "barrier" functions from the banal to those regulating reality adaptations, has been noticed, and the inability to ward off or put bounds around intrapsychic or external stimuli has been noted in the so-called "flashback" phenomenon. The model of the traumatic neuroses in which repetitive noxious experience recurs after the mastery of ongoing stimuli was unexpectedly disrupted (or the "stimulus barrier" breached), and the need to synthesize the intensities of experience, has been noted as a possible mechanism in this inconstantly occurring after effect of LSD or mescaline. The phenomena occurs generally briefly, and not as the lay imagination conceives it, as a miniature "rerun" of hours of a particular LSD episode; thresholds for observations of minor alterations of states of consciousness are often enhanced—both by publicity and perhaps by the drug experience—and the interpretation of these effects can lead to panic and excessive focus upon subjective states. In any event, the experience and its mastery during the drug state possibly accounts for the variability of outcomes, and certainly defines the chief characteristics of these states in which the operations of variables such as expectation, group structuring and reinforcement, and individual experience and coping, are strikingly revealed as both crucial and variable. It is nevertheless noteworthy

that animals can detect very low and behaviorally in apparent doses of these drugs and distinguish LSD from mescaline, for example. Accordingly, the neural and chemical mechanisms evoking these perceptions are of some interest in understanding brain function and psychotic like behaviors.

Initial comparisons of the LSD state with naturally occurring psychoses tended to conclude that the two were not related. Later comparisons have shown that some psychotic reactions can be characterized by the "psychedelic" form of experience which may accompany the use of LSD-like drugs. Cumulative-dose experiments performed with LSD-like compounds tend to produce tolerance unlike the effects in amphetamine experiments (in which psychosis supervenes). Response to and resistance to noxious stimuli after several days of LSD has not been systematically examined in man. In animals on tolerance dosage schedules, such stimuli can enhance or disrupt certain performances and apparently do not show tolerance. The LSD-precipitated psychotic reaction—an extended psychosis following LSD use—tends to be somewhat different from the amphetamine-induced psychoses. The former may be associated with more ecstatic elements and less routinely with psychotic suspiciousness. Drugs in these two classes also tend to produce different EEG effects in animals and these differences have led investigators to propose these drugs as prototypes of two distinct classes of psychotomimetic drugs. Whether the effects of cumulative doses of amphetamine (or the immediate as well as prolonged effects of acute doses of

methamphetamine) are linked to persisting effects of intermediate metabolites of the drug is not precisely known. The presence of LSD in the body can be roughly correlated with different phases in the drug response. For example, it is apparent that four to eight hours after the acute LSD effects (which correspond to the half-life of the drug in plasma), suspiciousness and ideas of reference are characteristic when the acute "TV show in the head" is over. It would be misleading to suggest, therefore, that the syndromes are distinctively different with the two drugs at the clinical level, as evident from the following example.

The patient was Nancy, a twenty-year-old female in her second year at college. She was basically rather easygoing but was particularly influenced by her father whom she described as a "man of principle," and who was frequently very critical of her. She took a summer trip alone and was given LSD by some travelers she met along the way. The psychosis which resulted was later described by Nancy during her recovery in the following manner:

I had spent the whole summer testing out life styles. So I decided to take a trip out west to see what I could learn from others. That's when I met this fellow Ray. I was fascinated by the life they lived—lots of drags and sex. I felt this was the opening up of sex for me. You have to understand that this was a complete change in life style for me, a new world completely. Some parts were beautiful. I took several capsules of acid over the two-week period and

began to see significance in things. They mentioned a dog and I thought I had become a dog sexually. Maybe, I thought, they were trying to teach me not to be up tight about sex. I began to have the notion that I would have a sex-change operation. Maybe I was a guy trapped in a woman's body. My mind was running like crazy. I thought I was adopted, maybe sterile or suffering from mental retardation. I saw a double rainbow and that made me believe there was hope. Noises were especially loud. Anything I ever had as a problem my mind dug up. Particularly problems with my father and with church. All the books I had ever read in my life seemed to come back to me. I thought I might have a terminal disease, be sterile or pregnant. So much was hitting my head at once. I often had a very strong urge to laugh. My body was supersensitive. I thought my bed would separate and that I would be torn in half, that the top half of me belonged to the devil and I would pay for what I had done. On my way to a hospital I noticed that everything behind me was being burned or destroyed. Again the idea of the atom bomb having been dropped came to me. I thought I would die and be reborn. In the hospital I thought one of the nurses was the devil. That meant I was split in quarters—half of me was a devil and half a woman. Also I was afraid to move for fear that something terrible would happen. I thought there was something registering my movements. I had an idea that I had to save the neighborhood. Sometimes I felt only capable of destruction, other times I thought I could save others.

Of particular significance in this kind of syndrome are the dynamic issues related to guilt and self-debasement. Such concerns have emerged repeatedly in cases we have seen and in reports of psychotic reactions related to LSD ingestion. In some ways the prolonged LSD-psychosis is similar, at least at the level of clinical analysis, to psychotic depression. Conflictual issues of guilt and shame seem uniquely heightened and thrust into awareness by these drugs. Long-term ingestion of LSD-like compounds may result in amotivational states which can be ego-syntonic and associated with atypical belief systems or delusional ideas.

Although the actual mechanism of action of LSD-like drugs is unknown, a remarkably reliable property of psychoactive drugs in this class is their biochemical and physiological effect upon 5-hydroxytryptamine-containing neurons. There is tentative evidence that psychotic reactions following LSD may be associated with decreased formation of 5-hydroxyindoleacetic acid, a metabolite of 5-hydroxytryptamine, in cerebrospinal fluid, a finding consistent with the neurochemical effect of acute administration of LSD-like drugs to animals. (See references 47, 50, and 86).

Cannabis

Although there has been some controversy concerning the psychotogenic potential of cannabis-containing compounds, the question,

apparently, is primarily one of dose. In countries where strong cannabis preparations are available, psychotic reactions are not uncommon (See references 58, 71, 73, 81, 94, 97, and 106). Although the basic pharmacology is somewhat different, the spectrum of psychotic reactions to cannabis compounds is quite similar to that seen in LSD-related psychoses. Under experimental conditions with human subjects, Jones has shown that higher doses of cannabis produce effects indistinguishable from LSD on many behavioral scales. An unusual study documents the strikingly increased incidence of quasi-schizophrenic psychoses in a group of American servicemen during a period when hashish usage was extensive. With high doses of the active ingredient, Ag-THC (delta-g-tetrahydrocannabinol) a number of LSD-like psychotomimetic effects occur, but the dysphoric episode is generally terminated by drowsiness—unlike LSD effects.

Experienced users are aware of paranoid like responses after unexpectedly high doses, i.e., a hypervigilance and ideas of reference. There are many features and factors in psychotic reactions to cannabis which require differentiation in future research. These include the role of prior state. Most studies, such as the report of Mayor LaGuardia's Committee on Marihuana in 1944, indicate a small incidence of paranoid reactions although a general harmlessness of the experience for most individuals. Paranoid reactions have been ascribed to the use of prepsychotic or vulnerable subjects. The role of active metabolites in any persisting effects and the role

of factors in both cumulative effects of moderately small, frequent dosages and of high dosage of the more potent hashish require further attention and clarification.

L-Dopa

Psychotic reactions following L-Dopa therapy for Parkinsonism occur in a substantial portion of treated patients. Perhaps because this population is an older one and often uses anticholinergic drugs in addition to

L-Dopa, a significant number of these reactions are associated with some of the symptoms of delirium. Although actual reports are rare according to Snyder, apparently L-Dopa can induce psychotic symptoms in a clear sensorium in some cases. L-Dopa can induce a manic reaction or exacerbate psychotic symptoms in individuals who have a prior history of manic and schizophrenic behavior. Celesia and Barr emphasize that patients with postencephalitic Parkinsonism appear most susceptible to the spectrum of psychoses induced by L-Dopa. The role of "prior state" (perhaps prior imbalances in neurohumoral storage and release involving receptors and systems reacting to acetylcholine, catecholamines, and indoleamines) recurs as an explanatory factor in individual response. Celesia and Barr describe the unique characteristics of central L-Dopa intoxication; namely, psychosis and various dyskinetic symptoms, particularly facial and lingual dyskinesias.

When LSD was given forty-eight hours following reserpine pretreatment, oculogyric crises and dystonia were observed. Interestingly, such dyskinetic and extrapyramidal syndromes have not been a prominent aspect to the amphetamine psychoses, although stimulation of dopamine receptors is thought to play a major role in the mediation of several components of the amphetamine psychoses. Preexisting receptor sensitivity may be a differentiating factor in the clinical manifestations of dopaminergic stimulation.

Drugs Used in the Treatment of Psychological Depression

The monoamine oxidase inhibitors and tricyclic antidepressants, compounds effective in the treatment of certain depressive syndromes, may be associated with acute psychotic reactions even when employed at the usual therapeutic doses, as illustrated by the following case.

Example. A 28-year-old man, depressed and seclusive for months, was treated with a monoamine oxidase inhibitor. After two weeks he became more verbal and less depressed. However, he soon began to be hyperactive, agitated, and grandiose as exemplified in the following excerpt from a letter he wrote at that time to a woman whom he had known only a few days and who had been frightened by his intensity:

Dear Jane: I know the reason you have run away from everyone and

from me, the man you said you would share everything openly with, who believed in you and who trusted you to keep your word, not to be childish or afraid, is because you had a difficult menstrual period for a week and a very upsetting one which both of us can't take. I pray desperately every night that you will phone me or come back to me for help. Do you think everything we ever said and did together meant *nothing* [his emphasis] or was *false* or *sinful?* Dear God in Heaven, give me strength to face this crisis. If Jane has sinned please let me take her sins as mine so that she may come to me or heaven, serene and unmolested. If Jane or any other girl I've known should need blood or eyes or even a heart, let them be compatible with mine that I may give my organs freely to them, though my worthless, homely self dies. Amen. ... I started excellent dancing lessons and want you to come. I brought you a six hundred dollar wedding night ceremony present, about a thousand dollars of clothes and apartment furnishings, and I've dusted my hope chest off to share with you alone.

This mania like state with elements of elation and depression subsided over several days following the withdrawal of the drug. Elation or psychotic suspiciousness may be observed in the course of tricyclic antidepressant drug treatment and tends to subside rapidly following drug withdrawal and antipsychotic drug therapy. In such cases one assumes that there is some innate proclivity to psychotic or manic states. These drugs have been shown to exacerbate psychotic symptoms in individuals who have been diagnosed as

schizophrenic. Tricyclic compounds, as noted above, also possess significant anticholinergic activity and may be associated with delirium. The clinical distinction between a primary manic or psychotic state versus delirium with psychosis during tricyclic therapy may be difficult, but can usually be made by noting the presence or absence of significant disorientation. It is sometimes possible to achieve useful antidepressant results without the recurrence of delirium by a reduction in dosage.

Treatment

The most important step in the treatment of drug-related psychotic episodes is proper diagnosis and removal of the offending drug when possible. With potent pharmacological substances so readily available, a drug-induced reaction should be part of the differential diagnosis of any acute psychotic syndrome. The role of careful history, of "mismatches" between factors such as current stress and prior adjustment and the current mental status, the presence of amnesia or delirioid features may occasionally help in this, although there are few clear-cut pathognomonic features. Conservative management is always indicated where diagnosis is in doubt. The classical principles involved in the treatment of drug-induced delirium apply here: protection of the individual, general nursing care, and a supportive, simplified environment. Unless a pharmacological addition to therapy is clearly indicated, it is wise to avoid compounding the trouble with yet another drug. Where hyperactive behavior is a problem, acute sedation with barbiturates may be as useful as phenothiazine administration. The important role of setting and psychological support for the treatment of psychotic drug reactions has recently been reemphasized. (It is a curious observation that psychotic reactions clearly related to drug use rarely evoke the same sympathy or therapeutic zeal in treatment personnel as do other psychotic states.) If the psychotic reaction is brief and essentially terminated within twenty-four hours one may be justified in providing acute treatment only.

However, if the reaction is prolonged or uniquely disturbing to the individual, responsible treatment should include several follow-up visits to determine whether characteristic defensive forces have been redeployed and to evaluate current life stresses the individual is facing which may have contributed to the dysphoric reaction. Where drug use initiates a psychotic process which seems to gain momentum and continue beyond the known duration of drug action, psychiatric hospitalization may be necessary. Flashbacks or related recurrent phenomena present interesting treatment problems in their own right. In general the therapeutic approach involves an avoidance of undue attention to the phenomena themselves and a focus upon attendant life tasks which are being avoided. Sedative antianxiety drugs or low doses of phenothiazines may be of some benefit as in other nonpsychotic conditions where symptom relief facilitates psychological work.

Bibliography

Abramson, H. A. in H. A. Abramson, ed., *Conference on Neuropharmacology,* Trans. 3rd Conf., p. 268. New York: Josiah Macy, Jr., Foundation, 1957.

Aghajanian, G. "Influence of Drugs on the Firing of Serotonin-Containing Neurons in Brain," *Fed. Proc.,* 31 (1972), 91-96.

Aghajanian, G. and O. Bing. "Persistence of Lysergic Acid Diethylamide in the Plasma of Human Subjects," *Clin. Pharmacol. Ther.,* 5 (1964), 611-614.

Anderson, E. "Propylhexedrine (Benzedrex) Psychosis," *N.Z. Med. J.,* 71 (1970), 302.

Angrist, A. and S. Gershon. "The Phenomenology of Experimentally Induced Amphetamine Psychosis-Preliminary Observations," *Biol. Psychiatry,* 2 (1970), 95-107.

Angrist, B., J. Schweitzer, A. Friedhoff et al. "The Clinical Symptomatology of Amphetamine Psychosis and Its Relationship to Amphetamine Levels in Urine," *Int. Pharmacopsychiatry,* 2 (1969), 125-139.

Angrist, B., J. Schweitzer, S. Gershon et al. "Mephentermine Psychosis: Misuse of the Wyamine Inhaler," *Am. J. Psychiatry,* 126 (1970), 1315-1317.

Angrist, B., B. Shopsin, and S. Gershon. "Comparative Psychotomimetic Effects of Stereoisomers of Amphetamine," *Nature,* 234 (1971), 152-153.

Baldessarini, R. and R. Willmuth. "Psychotic Reactions During Amitriptyline Therapy," *Can. Psychiatr. Assoc. J.*, 13 (1968), 571-573.

Bass, M. "Sudden Sniffing Death," *JAMA,* 212 (1970), 2075-2079.

Bell, D. "A Comparison of Amphetamine Psychosis and Schizophrenia," *Br. J. Psychiatry,* 3 (1965), 701-706.

----. "The Experimental Reproduction of Amphetamine Psychosis," *Arch. Gen. Psychiatry,* 29 (1973). 35-45.

Bethell, M. “Toxic Psychosis Caused by Radioactive Iodine,” *Br. J. Psychiatry,* 117 (1970), 473-479

Blacker, K., R. Jones, G. Stone et al. “Chronic Users of LSD: The ‘Acidheads’,” *Am. J. Psychiatry,* 125 (1968), 341-351.

Blatherwick, C. “Understanding Glue Sniffing,” *Can. J. Public Health,* 63 (1972), 272-276.

Bowers, M. “Acute Psychosis Induced by Psychotomimetic Drug Abuse,” *Arch. Gen. Psychiatry,* 27 (1972), 437-442.

Bowers, M., A. Chipman, A. Schwartz et al. “Dynamics of Psychedelic Drug Abuse,” *Arch. Gen. Psychiatry,* 16 (1967), 560-565.

Bowers, M. and D. Freedman. “‘Psychedelic’ Experiences in Acute Psychoses,” *Arch. Gen. Psychiatry,* 15 (1966), 240-248.

Bowers, M., E. Goodman, and V. Sim. “Some Behavioral Changes in Man Following Anticholinesterase Administration,” *J. Nerv. Ment. Dis.,* 138 (1964), 383-389.

Bowers, M. and D. Singer. “Thyrotoxicosis and Psychological State,” *Psychosomatics,* 5 (1964), 322-324.

Braceland, F. “Mental Symptoms following Carbon Disulphide Absorption and Intoxication,” *Ann. Intern. Med.,* 16 (1942), 246-261.

Brawley, P. and J. Duffield. “The Pharmacology of Hallucinogens,” *Pharmacol. Rev.,* 24 (1972), 31-66.

Bridger, W. “Psychotomimetic Drags, Animal Behavior, and Human Psychopathology,” in J. O. Cole, A. M. Freedman, and Friedhoff, eds., *Psychopathology and Psychopharmacology,* pp. 133—142. Baltimore: The Johns Hopkins University Press, 1973.

Bridger, W. and I. Mandel. “Excitatory and Inhibitory Effects of Mescaline on Shuttle Avoidance in the Rat,” *Biol. Psychiatry,* 3 (1971), 379-385.

Cameron, O. “Stimulus Properties of Drugs: LSD as SD and UCS,” Dissertation, University of Chicago, August 1972.

Celesia, G. and A. Barr. “Psychosis and Other Psychiatric Manifestations of Levodopa Therapy,” *Arch. Neurol.,* 23 (1970), 193-200.

Celesia, G. and W. Wanamaker. “Psychiatric Disturbances in Parkinson’s Disease,” *Dis. Nerv. Sys.,* 33 (1972), 577-583.

Clark, L., W. Bauer, and S. Cobb. “Preliminary Observations on Mental Disturbances Occurring in Patients Under Therapy with Cortisone and ACTH,” *N. Engl. J. Med.,* 246 (1952), 205-216.

Connell, P. Amphetamine Psychosis. Maudsley Monogr. no. 5, p. 5. London: Oxford University Press, 1958.

Crowell, E. and J. Ketchum. “The Treatment of Scopolamine-Induced Delirium with Physostigmine,” *Clin. Pharmacol. Ther.,* 8 (1967), 409-414.

Daly, R., F. Kane, and J. Ewing. “Psychosis Associated with the Use of a Sequential Oral Contraceptive,” *Lancet,* 2 (1967), 444-445.

Damasio, A., J. Lobo-Antunes, and Macedo. “Psychiatric Aspects in Parkinsonism Treated with L-Dopa,” *J. Neurol. Neurosurg., Psychiatry,* 34 (1971), 502-507.

Domino, E. F. “Neurobiology of Phencyclidine (Sernyl), a Drug with an Unusual Spectrum of Pharmacological Activity,” *Int. Rev. Neurobiol.,* 6 (1964), 303-347.

Domino, E. F. and E. Luby. “Abnormal Mental States Induced by Phencyclidine as a Model of Schizophrenia,” in J. O. Cole, A. M. Freedman, and A. Friedhoff, eds., *Psychopathology and Psychopharmacology,* pp. 37-50. Baltimore: The Johns Hopkins University Press, 1973.

Duvoisin, R. and R. Katz. “Reversal of Central Anticholinergic Syndrome in Man by Physostigmine,” *JAMA,* 206 (1968), 1963-1965.

Edison, G. “Hallucinations Associated with Pentazocine,” *N. Engl. J. Med.,* 281 (1969), 447-448.

Elkes, J. “Effects of Psychotomimetic Drags in Animals and Man,” in H. A. Abramson, ed., *Conference on Neuropharmacology,* Trans. 3rd. Conf., pp. 205-295. New York: Josiah Macy, Jr., Foundation, 1957.

Ellinwood, E. “Amphetamine Psychosis 1: Description of the Individuals and Process,” *J. Nerv. Ment. Dis.,* 44 (1967), 273-280.

----. “Effect of Chronic Methamphetamine Intoxication in Rhesus Monkeys,” *Biol. Psychiatry,* 3 (1971), 25-32.

----. “Assault and Homicide Associated with Amphetamine Abuse,” *Am. J. Psychiatry,* 127 (1971), 1170-1175.

Ellinwood, E. and O. Escalante. “Behavior and Histopathological Findings During Chronic Methedrine Intoxication,” *Biol. Psychiatry,* 2 (1970), 27-39.

Ellinwood, E., A. Sudilovsky, and L. Nelson. “Behavioral Analysis of Chronic Amphetamine Intoxication,” *Biol. Psychiatry,* 4 (1972). 215-230.

Erikssen, J. “Atropine Psychosis,” *Lancet,* 1 (1969), 53-54.

Escalante, O. and E. Ellinwood. “Central Nervous System Cytopathological Changes in Cats with Chronic Methedrine Intoxication,” *Brain Res.,* 21 (1970), 151-155.

Flowers, N. and L. Horan. “The Electrical Sequelae of Aerosol Inhalation,” *Am. Heart J.,* 83 (1972), 644-651.

----. “Nonanoxic Aerosol Arrhythmias,” *JAMA,* 219 (1972), 33-37-

Freedman, D. “Studies of LSD-25 and Serotonin in the Brain,” *Proc. 3rd World Congr. Psychiatry,* 1 (1961), 653-658.

----. “On the Use and Abuse of LSD,” Arch. Gen. Psychiatry, 18 (1968), 330-347.

Freedman, D. and N. Giarman. “Brain Amines, Electrical Activity, and Behavior,” in G. H. Glaser, ed., *EEG and Behavior,* pp. 198-243. New York: Basic Books, 1963.

Freedman, D., R. Gottlieb, and R. Lovell. “Psychotomimetic Drugs and Brain 5-Hydroxytryptamine Metabolism,” *Biochem. Pharmacol.,* 19 (1970), 1181-1188.

Gershon, S. and B. Angrist. “Drug-Induced Psychoses,” *Hosp. Practice,* 2 (1967), 36-39, 50-53.

Giarman, N. and D. Freedman. “Biochemical Aspects of the Actions of Psychotomimetic Drugs,” *Pharmacol. Rev.,* 17 (1965), 1-25.

Glass, G. and M. Bowers. “Chronic Psychosis Associated with Long-Term Psychotomimetic Drug Abuse,” *Arch. Gen. Psychiatry,* 23 (1970), 97-103.

Gonzales, E. and J. Downey. “Polyneuropathy in a Glue Sniffer,” *Arch. Phys. Med. Rehahil.,* 53 (1972), 333-337-

Goodwin, F. “Psychiatric Side Effects of Levodopa in Man,” *JAMA,* 218 (1971), 1915-1920.

Gordy, S. and M. Thumper. “Carbon Disulfide Poisoning with a Report of Six Cases,” *JAMA*, 110 (1938), 1543-1549.

Griffith, J., J. Cavanaugh, J. Held et al. “Dexroamphetamine-Evaluation of Psychotomimetic Properties in Man,” *Arch. Gen. Psychiatry,* 26 (1972), 97-100.

Grossman, W. “Adverse Reactions Associated with Cannabis Products in India,” *Ann. Intern. Med.,* 70 (1969), 529-533.

Hedley, A. and P. Bewsher. “Psychosis and Antithyroid Drug Therapy,” *Br. Med. J.,* 3 (1969), 596-597.

Hoch, P., J. Cattell, and H. Pennes. “Effects of Mescaline and LSD,” *Am. J. Psychiatry,* 108 (1952), 579-584.

Hoff, E. “Brain Syndromes Associated with Drug or Poison Intoxication,” in A. Freedman and H. Kaplan, eds., *Comprehensive Textbook of Psychiatry,* pp. 759-775. Baltimore:

Williams & Wilkins, 1967.

Hollister, L. Chemical Psychosis. Springfield, Ill.: Charles C. Thomas, 1968.

Hollister, L., R. Richards, and H. Gillespie. "Comparison of Tetrahydrocannabinol and Synbexyl in Man," *Clin. Pharmacol. Ther.,* 9 (1969), 783-791.

Horn, A. and S. Snyder. "Chlorpromazine and Dopamine: Conformational Similarities that Correlate with the Antischizophrenic Activity of Phenothiazine Drugs," *Proc. Natl. Acad.* Sci. USA, 68 (1971), 2325-2328.

Hussain, M. and J. Murphy. "Psychosis Induced by Oral Contraception," *Can. Med. Assoc. J.,* 104 (1971), 984-986.

Isbell, H., R. E. Belleville, and H. F. Fraser. ''Studies on Lysergic Acid Diethylamide (LSD-25)," *Arch. Neurol. Psychiatry,* 76 (1956), 468-478.

Isbell, H., A. B. Wolbach, A. Winkler et al. "Cross Tolerance Between LSD and Psilocybin," *Psychopharmacologia,* 2 (1961), 147-159.

Janowsky, D., M. El-Yousef, J. Davis et al. "Provocation of Schizophrenic Symptoms by Intravenous Methylphenidate," *Arch. Gen. Psychiatry,* 28 (1973), 185-193.

Jones, R. "Drug Models of Schizophrenia—Cannabis," in J. O. Cole, A. M. Freedman, and A. Friedhoff, eds., *Psychopathology and Psychopharmacology,* pp. 71-86. Baltimore: The Johns Hopkins University Press, 1973.

Kane, F. and R. Florenzano. "Psychosis Accompanying Use of Bronchodilator Compound," *JAMA,* 215 (1971), 2116.

Keup, W. "Psychotic Symptoms Due to Cannabis Abuse," *Dis. Nerv. Syst.,* 31 (1970), 119-126.

Kimura, E., D. Ebert, and P. Dodge. "Acute Toxicity and Limits of Solvent Residue for Sixteen Organic Solvents," *Toxicol. Appl. Pharmacol.,* 19 (1971), 699-704.

Klee, G. "Marihuana Psychosis—a Case Study," *Psychiatr. Q.,* 43 (1969), 719-733.

Levin, M. "Transitory Schizophrenias Produced by Bromide Intoxication," *Am. J. Psychiatry,* 103 (1946), 229-237.

----. "Bromide Psychosis: Four Varieties," *Am. J. Psychiatry,* 104 (1948), 798-800.

Lidden, S. and R. Satran. "Disulfiram (Antabuse) Psychosis," *Am. J. Psychiatry,* 123 (1967), 1284-1289.

Louria, D., T. Hensle, and J. Rose. "The Major Medical Complications of Heroin Addiction," *Ann. Intern. Med.,* 76 (1967), 1-22.

Luby, E., B. Cohen, G. Rosenbaum et al. "Study of a New Schizophrenomimetic Drag-Sernyl," *Arch. Neurol. Psychiatry,* 81 (1959), 113-119.

Meyer, J., F. Greifenstein, and M. Devault. "A New Drug Causing Symptoms of Sensory Deprivation," *J. Nerv. Ment. Dis.,* 129 (1959), 54-61.

Newell, H. and T. Lidz. "The Toxicity of Atabrine to the Central Nervous System," *Am. J. Psychiatry,* 102 (1946), 805-818.

Perna, D. "Psychotogenic Effect of Marihuana," *JAMA,* 209 (1969), 1085-1086.

Quarton, G., L. Clark, S. Cobb et al. "Mental Disturbances Associated with ACTH and Cortisone," *Medicine* (Baltimore), 34 (1955), 13-50.

Redlich, F. and D. Freedman. *The Theory and Practice of Psychiatry,* p. 741. New York: Basic Books, 1966.

Reich, P. and R. Hepps. "Homicide During a Psychosis Induced by LSD," *JAMA,* 219 (1972), 869-871.

Rome, H. and F. Braceland. "Psychological Responses to Corticotropin, Cortisone, and Related Steroid Substances," *JAMA,* 148 (1952), 27-30.

Rosecrans, J., R. Lovell, and D. Freed man. "Effects of Lysergic Acid Diethylamide on the Metabolism of Brain 5-Hydroxytryptamine," *Biochem. Pharmacol.,* 16 (1967), 2011-

2021.

Salvatore, S. and R. Hyde. “Progression of Effects of LSD,” *Arch. Neurol. Psychiatry,* 76 (1956), 50-59.

Shick, J. and D. Smith. “Analysis of the LSD Flashback,” J. Psychedel. Drugs, 3 (1970), 13-19.

Shilliro, F., C. Drinker, and T. Shaughnessy. “The Problem of Nervous and Mental Sequelae in Carbon Monoxide Poisoning,” *JAMA,* 106 (1936), 669-674.

Smith, D. “An Analysis of 310 Cases of Acute High-Dose Methamphetamine Toxicity in Haight-Ashbury,” *Clin. Toxicity,* 3 (1970), 117-124.

Snyder, S. “Catecholamines in the Brain as Mediators of Amphetamine Psychosis,” *Arch. Gen. Psychiatry,* 27 (1972), 169-179.

Snyder, S., K. Taylor, J. Coyle et al. “The Role of Brain Dopamine in Behavioral Regulation and the Actions of Psychotropic Drugs,” *Am. J. Psychiatry,* 127 (1970), 199-207.

Soskis, D. and M. Bowers. “The Schizophrenic Experience—A Follow Up Study of Attitude and Posthospital Adjustment,” *J. Nerv. Ment. Dis.,* 149 (1969), 443-449.

Spencer, D. “Cannabis Induced Psychosis,” *Br. J. Addict.,* 65 (1970), 369-372.

Spensley, J. and D. Rickwell. “Psychosis during Methylphenidate Abuse,” *N. Engl. J. Med.,* 286 (1972), 880-881.

Stockings, G. “A Clinical Study of the Mescaline Psychosis, with Special Reference to the Mechanism of the Genesis of Schizophrenic and Other Psychotic States,” *J. Ment. Sci.,* 86 (1940), 29-47.

Talbott, J. and J. Teague. “Marihuana Psychosis,” *JAMA,* 210 (1969), 299-302.

Taylor, R., J. Maurer, and J. Tinklenberg. “Management of ‘Bad Trips’ in an Evolving Drug Scene,” *JAMA,* 213 (1970), 421-425.

Tennant, F. and C. Groesbeck. “Psychiatric Effects of Hashish,” *Arch. Gen. Psychiatry,* 27 (1972), 133-136.

Thomas, D. and D. Freedman. “Treatment of the Alcohol Withdrawal Syndrome,” *JAMA,* 188 (1964), 316-318.

Ullman, K. and R. Groh. “Identification and Treatment of Acute Psychotic States Secondary to the Usage of Over-the-Counter Sleeping Preparations,” *Am. J. Psychiatry,* 128 (1972), 1244-1248.

Victor, M. and R. Adams. “The Effect of Alcohol on the Nervous System,” *Assoc. Res. Nerv. Ment. Dis. Proc.,* 32 (1953), 526-573.

Wallach, M., R. Angrist, and S. Gershon. “The Comparison of the Stereotyped Behavior-Inducing Effects of d- and 1-Amphetamine in Dogs,” *Comm. Behav. Biol.,* 6 (1971). 93-96.

Wallach, M., E. Friedman, and S. Gershon. “2,5-Dimethoxy-4-Methylamphetamine (DOM), a Neuropharmacological

Examination,” *J. Pharmacol. Exp. Ther.,* 182 (1972), 145-154.

Wallach, M. and S. Gershon. “A Neuro-psychopharmacological Comparison of D-Amphetamine, L-Dopa, and Cocaine,” *Neuropharmacology,* 10 (1971), 743-752.

Weil, A. “Adverse Reactions to Marihuana,” *N. Engl. J. Med.,* 282 (1970), 997-1000.

Weil-Malherbe, H. and S. Szara. *The Biochemistry of Functional and Experimental Psychoses*. Springfield, Ill.: Charles Thomas, 1971.

Weinstein, M. and A. Fischer. “Benztropine Toxicity and Atropine Psychosis,” *JAMA,* 220 (1972), 1616-1617.

Yost, M. and F. McKegney. “Organic Psychosis Due to Talwin (Pentazocine),” *Conn. Med.,* 34 (1970), 259-260.

Young, D. and W. Scoville. “Paranoid Psychosis in Narcolepsy and the Possible Dangers of

Benzedrine Treatment," *Med. Clin. North Am.,* 22 (1938), 637-646.