National Institute on Drug Abuse

Research 21

MONOGRAPH SERIES

PCP

Phencyclidine Abuse: An Appraisal

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES • Public Health Service • Alcohol, Drug Abuse, and Mental Health Administration

Phencyclidine (PCP) Abuse: An Appraisal

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NIDA Research Monograph 21

August 1978

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Alcohol, Drug Abuse, and Mental Health Administration

National Institute on Drug Abuse
5600 Fishers Lane
Rockville, Maryland 20857

NIDA Research Monographs are prepared by the research divisions of the National Institute on Drug Abuse and published by its Office of Science. The primary objective of the series is to provide critical reviews of research problem areas and techniques, the content of state-of-the-art conferences, and integrative research reviews Its dual publication emphasis is rapid and targeted dissemination to the scientific and professional community.

Parklawn Building, 5600 Fishers Lane, Rockville, Maryland 20857

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ACKNOWLEDGMENT

This monograph is based upon papers presented at a conference which took place on February 27-28, 1978, at the Asilomar Conference Center, Pacific Grove, California. The conference was conducted and reported by PLOG Research, Inc. , Reseda, California under NIDA contract 271-77-3413.

Library of Congress catalog card number 78-600095

DHHS publication number (ADM) 85-728
Printed 1978 Reprinted 1983, 1985

NIDA Research Monographs are indexed in the Index Medicus. They are selectively included in the coverage of American Statistics Index, BioSciences Information Service, Chemical Abstracts, Current Contents , Psychological Abstracts , and Psychopharmacology Abstracts

Foreword

Phencyclidine (PCP), or “angel dust” as it is more commonly known to drug users, posed until recently a relatively modest problem. While some illicit use occurred as early as the mid ‘6Os, the drug’s initially poor street reputation seemed to make it decidedly unlikely that it would ever become popular as a drug of choice.

More recent events have made it abundantly clear that our initial optimism was poorly founded. A change in mode of use from oral ingestion to smoking or snorting, which may enable the user to better control aversive consequences of use, together with the ease with which PCP can be synthesized, have markedly changed the phencyclidine abuse picture.

In one year (from 1976 to 1977) the number who had used phencyclidine as measured by NIDA’s National Drug Use Surveys nearly doubled in the 12 to 17 year age group. Among young adults between 18 and 25, the number of PCP users increased nearly fifty percent in that same year. Although the level of use detected was still modest, there is good reason to believe that the standardized indicators of the extent of PCP use and of its adverse consequences represent significant under-estimates of the seriousness of the problem. Clinical reports have also indicated that phencyclidine use can precipitate violent acting out and seriously self-destructive behavior as well as psychotic thinking and behavior.

Because of the relatively recent emergence of phencyclidine abuse as a problem of widespread proportions, our knowledge remains fragmentary. If the dimensions of the problem continue to be in doubt, still more remains to be learned about the implications of use, especially on a chronic basis. This volume represents an attempt to bring together our present knowledge. It is based on a small working conference of researchers and clinicians with extensive PCP experience which was held in late February of this year (1978). We hope that it proves to be a useful compendium of information on the problem as well as a stimulus to further work to answer some of the critical questions with which we are confronted. In addition, because phencyclidine may well prove to be prototypic of a range of easily synthesized psychoactive drugs susceptible to abuse, we hope it will stimulate thinking about better ways both to anticipate newly emerging drug problems and to cope with them.

The Editors

Contents

Chapter 1

Phencyclidine: An Overview

Robert C. Petersen, Ph.D., and Richard C. Stillman, M.D.

Although phencyclidine was first abused in oral form over a decade ago, it is only in recent years as a smoked or snorted drug that it has become a more serious problem involving significant numbers of users. This overview is intended to review and summarize what is presently known about the drug with special emphasis on the contributions of the authors of this volume. By providing a relatively brief integrated view of our current knowledge we hope to convey the limitations of that knowledge and to encourage others to enlarge our presently modest understanding of the implications of phencyclidine abuse.

THE MATERIAL

Phencyclidine,or PCP, one of the group of arylcyclohexylamines, is in pharmaceutically pure form a white powder which readily dissolves in water. In "street" form PCP is often adulterated and quite often misrepresented as a variety of other drugs. It is highly variable in appearance, being sold in liquid, powder, and tablet form, the latter two in many colors. As a powder or liquid, it is often placed on parsley or on other leaf mixtures to be smoked as cigarettes (joints). When misrepresented, PCP is most commonly sold as THC (the principal psychoactive ingredient in marihuana, which in reality is not available on the street). But phencyclidine has also been sold as cannabinol (another marihuana constituent), mescaline, psylocybin, LSD, and even as amphetamine or cocaine. Because of the variability in street names and its frequent misrepresentation, the casual user may be unaware of what he or she has ingested or may be mistaken about its true identity.

Some of the street names for phencyclidine include: angel dust, dust, crystal, cyclones, embalming fluid, elephant or horse tranquilizer, killer weed, superweed, mintweed, mist, monkey dust, Peace Pill, rocket fuel, goon, surfer, KW, and scuffle. The wide range of regional names for this illicit drug, as well as variations in its appearance, mean that the casual user may not be aware that he or she has used PCP or may fail to report its use in surveys because he or she does not know the drug by the survey designation. A further complication in user identification of PCP is the fact that phencyclidine is sometimes also used in combination with such other drugs as barbiturates, heroin, cocaine, amphetamine, methaqualone, LSD, mescaline, and procaine (cf. Lerner and Burns, this volume).

Depending on the care with which the synthesis of PCP is carried out, the street drug may contain a variety of impurities, including potassium cyanide. Although PCP is sometimes smoked after sprinkling it on marihuana, it is apparently rarely sold in that combination. At least one major laboratory on the West Coast which does street drug analysis has never encountered the combination in samples submitted to it.

In addition to phencyclidine itself, there are over thirty chemically similar analogs, some of which are capable of producing similar psychic effects. These also can be synthesized with varying degrees of difficulty, and some have already appeared on the street. Those reportedly abused thus far include: PCC, PCE, PHP, TCP, and the anesthetic, ketamine . Details of their chemical formulas and structure are given by Domino (this volume) . The addition of these compounds, and possibly others in the future, makes the problem of “tracking" PCP and related drug use more difficult.

Adding to the risk of PCP use, especially when it is taken orally, is the wide variability in purity of the street drug. Even when it is not misrepresented, the percentage of PCP contained in street samples has been found to be quite variable.

When PCP is sold as a granular powder (“angel dust”), it is usually relatively pure, consisting of perhaps 50-100 percent phencyclidine. However, sold under a variety of other names and/or in other forms, the purity is from 5 to 30 percent, with leafy mixtures generally containing the smallest amounts of the drug. While in the past street samples of phencyclidine have often been found on analysis to contain other drugs as well, more recently such samples appear less likely to contain other drugs in addition to PCP. It should, of course, be noted that samples submitted by users for analysis are not necessarily representative of street drugs overall. Users are far more likely to have analyzed drugs about which they have some doubt or from which they have had some unusual reaction. Nevertheless, it does appear that the purity of PCP street samples has increased in that it is less frequently sold mixed with other psychoactive materials.

Phencyclidine can be easily synthesized. The “starting” chemicals are widely available and because of their important industrial uses do not lend themselves to more stringent controls. While some of the mass media accounts have exaggerated the ease with which phencyclidine can be made. it is not particularly difficult and can be done by individuals with only modest technical training and without elaborate equipment.

The precise classification of PCP is presently unsettled. PCP has stimulant, depressant, hallucinogenic, and analgesic properties which are dose-dependent. One proposed classification is with ketamine as a "dissociative anesthetic" (cf. Domino, this volume).

Phencyclidine is used legally in veterinary medicine as an animal immobilizing agent. Although it was originally developed as an anesthetic for use with humans, it was later abandoned for that purpose because in some patients it produced post-operative thought disturbances and agitation. PCP made its first illicit appearance in 1965 on the West Coast. At that time it rapidly developed a bad street reputation and had only limited popularity. Since then there have been sporadic outbreaks of its use. Most recently there is evidence from a variety of sources suggesting a marked increase in use (cf. Extent of Phencyclidine Abuse, below).

Although originally orally ingested, PCP is now most commonly smoked or snorted. Intravenous use is much less frequent, but has been reported. By smoking, the experienced user is better able to limit his dose (self-titrate) to a level with which he or she is comfortable and is probably less likely to overdose. By contrast, when the drug is taken by mouth there is a longer period before the drug takes effect, it continues to be absorbed after the user may have concluded he has had enough, and the dose is frequently larger--all factors more likely to result in adverse reactions due to an overdose.

BIOLOGICAL, NEUROCHEMICAL, AND PRECLINICAL BEHAVIORAL ASPECTS

Three of the papers in this volume focus specifically on what is presently known about the neurobiological, neurochemical, and preclinical behavioral aspects of phencyclidine. Domino (this volume) divides and summarizes the major pharmacological properties of PCP and related compounds as follows:

Central Nervous System Effects

a. Small doses lead to a "drunken" state with numbness of the extremities and in some species produces excitation.
b. In moderate doses, analgesia and anesthesia are produced.
c. A psychic state somewhat resembling sensory isolation is produced. Sensory impulses in grossly distorted form do, however, reach the neocortex.
d. Cataleptiform motor responses occur.
e. Large doses, expecially of PCP, may produce convulsions.
f. There are marked inter-species differences in effects. Primates and especially man show predominantly depressant effects.

Autonomic and Cardiovascular System Effects

a. Sympathomimetic effects are produced including increases in heart rate and blood pressure.
b. Catecholamines are potentiated through a cocaine-like action.

Balster and Chait (this volume) in their review of the preclinical behavioral pharmacology of PCP emphasize several points. They too underscore the interspecies differences in PCP effects. For example, in rodents, unlike primates, PCP has excitatory rather than depressant effects.

Unlike virtually all other hallucinogens, with which PCP is sometimes categorized, monkeys will self-administer phencyclidine. This suggests that animal testing of other PCP analogs may be useful in predicting their dependence liability in man. Experiments with PCP to date do not, however, suggest that phencyclidine produces comparable physical dependence to that of the opiates or other CNS depressants. Tolerance from two to four times the original amounts develops if the drug is administered chronically to test animals. Finally, work done thus far indicates the PCP enhances the depressant effects of delta-9-THC (the principal psychoactive ingredient in marihuana) and the anesthetic effects of pentobarbital. When administered with d-amphetamine, there is preliminary evidence that PCP increases amphetamine stereotype in rats.

Johnson, in his review of the neurochemical pharmacology of phencyclidine (this volume), emphasizes that our knowledge in this area is in its infancy, but that it appears unlikely that the diverse spectrum of effects is mediated by PCP's action on any one neurotransmitter. He also points out that there have been virtually no studies exploring the neurochemistry of chronic use.

EXTENT OF PHENCYCLIDINE ABUSE

Attempts at estimating the extent of PCP use are fraught with difficulty. Since the drug is often sold as any one of a variety of other psychoactive substances, the user, especially if he or she is inexperienced, may not realize PCP is involved. The fact that phencyclidine is known by an unusually large number of street names and varies widely in its physical appearance also contributes to confusion in casual user identification. Most official reports of drug use have in the past lumped PCP with other hallucinogens, making trend detection from such sources difficult. Moreover, the patient admitted for emergency treatment of PCP-induced bizarre behavior is likely to be diagnosed as acutely schizophrenic rather than as a toxic drug reaction. Patients admitted with injuries from automobile accidents, fires and drownings in which PCP was a cause may not be so identified. Thus a marked increase in use and in use-related drug emergencies may not be reflected in emergency room or medical examiner statistics.

Despite these limitations, there are a number of converging lines of evidence suggesting increased use in recent months. These range from reports of law enforcement agencies on disruption of illegal laboratory production to self-reports by users. While available survey data has definite limitations, they provide minimal estimates of the level of phencyclidine use as well as some short term trend indicators. In NIDA's 1976 National Survey, 3 percent of youth between 12 and 17 years of age at the time of the survey acknowledged having used PCP at some time in their lives. Among young adults 18-25, the age category in which virtually all drug use peaks, nearly one in ten reported having used PCP prior to the 1976 survey. By contrast, data from the 1977 National Survey suggests that the percentage who had ever used in the 12-17 year-old group had nearly doubled since the earlier survey (5.8 percent vs. 3.0 percent in 1976).

Use by the 18-25 age group had also increased markedly, from 9.5 percent to 13.9 percent. The likelihood that these increases were simply the result of year to year survey sampling variation is small (less than one in a hundred).

Some indication of the extent to which a drug poses serious problems is provided by the Government's Drug Abuse Warning Network (DAWN). DAWN is a national reporting system which collects reports of drug-related deaths and drug-related emergencies involving hospital emergency room treatment. For reasons that have already been outlined, such figures are likely to be minimal estimates of the overall PCP problem. They are, however, also useful in providing some indication of trends. When data are examined from the 662 emergency rooms which consistently reported to DAWN from November 1974 to October 1976, the rate of PCP emergencies doubled during that period (there were 111 mentions in October 1976 contrasted with 54 in October 1974). Reports of PCP-related deaths show nearly as great an increase when the period from April 1976 to March 1977 is contrasted with that of the previous year (30 PCP-related deaths vs. 17 the year before). Again, such figures are likely to be minimal estimates of the actual extent of PCP-related mortality.

A major reported cause of PCP deaths in California has been drowning. In one series of 19 PCP deaths investigated in two California counties, 11 of the 19 were from drowning--one while in the shower. The PCP user readily loses his orientation while swimming or immersed and frequently drowns, sometimes in very small amounts of water. Unless PCP in the body is specifically searched for under such circumstances, it is very likely to be missed. Similarly, deaths resulting from violent behavior and accidental deaths resulting from PCP intoxication may not be reported as PCP-related. Suicide while under the influence of the drug was the cause of death of three additional persons in the California study. Another death was the result of threatening behavior leading to the individual's being shot (Burns and Lerner 1978).

Another source of data which provides some indication of the extent of phencyclidine use among chronically drug-using youth is the National Youth Polydrug Study (NYPS), in which 97 drug abuse treatment programs specializing in treating youthful drug abusers participated. During the period from September 1976 to March 1977 interviews were conducted collecting detailed data on patterns of drug abuse for 2750 new clients under age 19. Within this sample nearly a third (31.8 percent) reported having ever used PCP. It was more often used than inhalants, sedatives, cocaine and opiates (other than heroin and methadone). Females in the sample were as likely to have used PCP as males. Whites were far more likely to report using it than either black or Hispanic clients (42.3 percent of whites, 8.5 percent of blacks and 9.0 percent of Hispanics). Females in the sample were found to have first used PCP at a slightly earlier age (14.4 years) than males (14.7 years). American Indians began use at the earliest age (13.9) followed by Hispanics (14.0) whites (14.6) and blacks, (15.3). Two-thirds of those who reported ever having used PCP reported continuing use at a rate of at least once a week for at least one month. PCP users had also used twice as many other recreational drugs as had non-PCPusers (6.0 vs. 2.8 substances respectively). Half the current PCP users were using PCP once a week or more often during the three month period that was studied. While this data source is obviously not representative of youth generally, it does suggest that PCP use is quite common among abusers of other drugs.

THE SUBJECTIVE EXPERIENCE -- MOTIVES FOR PHENCYCLIDINE USE

One of the more puzzling questions about PCP use is just why users continue to use in the light of the widely noted and even user acknowledged negative aspects of the experience. Several of the papers in this volume provide some insight into this important question both on the basis of user reports and on theoretical grounds. One answer that emerges is that initial reports both in the clinical literature and in the mass media have stressed the negative aspects and failed to note user-perceived more positive aspects. In a major study of some 319 adult users ranging in age from 21 to 38, Siegel (this volume) specifically questioned users regarding the subjective effects of the phencyclidine experience. Interestingly enough, users in this sample reported negative or undesired aspects on every occasion of PCP use and positive or desired effects of use, only 60 percent of the times used. Effects reported positively included heightened sensitivity to outside stimuli (by 94 percent of users), stimulation (92 percent), dissociation (88 percent), mood elevation (61 percent), inebriation (55 percent), and relaxation or tranquilization (by 55 percent of users). Only one in twelve (8 percent) reported experiencing euphoria, however. Negative effects reported by the majority of users included perceptual disturbances (by 75 percent), restlessness (by 76 percent), disorientation (63 percent), and anxiety (61 percent). Approximately a quarter to a third of users reported such troublesome effects as paranoia (34 percent), hyperexcitability (27 percent), irritability (22 percent), and mental confusion (22 percent). Four out of five users had speech difficulties (dysarthria) while using the drug. Fauman and Fauman (this volume) studied twenty-five chronic phencyclidine users under treatment in an Illinois residential treatment program. Their average age was nearly nineteen (18.8 years), and they had used PCP for an average of 3.6 years. Half (12) described their initial PCP experience in such positive terms as "fantastic," "mind blowing," an intense high or a happy experience. Ten of the twenty-five found the first experience neutral or mildly unpleasant. Only seven of the twenty-five reported their typical PCP experience was positive. Eleven reported their usual PCP experience to be unpleasant and three described it as making them feel "rowdy" or 'Violent." Lerner and Burns (this volume) in a study of 20 chronic users in the San Francisco area, report that four out of five found their first PCP experience "fun" "exhilarating," and that they (the users) felt "happy" or "euphoric." Marsella and Hicks (this volume) emphasize the role of drug use among native Hawaiian youth in the Job Corps as a way of relieving boredom and the possible importance of the drug experience in fostering a new sense of what is "real" in contrast to the more usual conceptions of non-drug using groups. Given this new normative standard, continued drug use may be important in maintaining it.

A theoretical framework for explaining the persistence of PCP-using behavior despite its obviously negative aspects is offered by Mello (this volume). She emphasizes the reinforcement value of the drug experience regardless of certain aversive consequences because of its role in changing the user's subjective state. In practical terms this means that a drug which has the ability to markedly alter the individual's subjective feelings may be reinforcing even though that alteration is not always marked by positive aspects in the usual sense.

Another aspect of the PCP experience that may be important in its continued use is the very risk taking it entails. The excitement of not knowing just how the experience will turn out and the ability to later boast of the risks taken, may convey a certain amount of status, especially in drug-using peer groups (perhaps in a way analogous to the telling of "war stories" by those who have been in the military). Related and perhaps easier to understand are some of the other effects reported by many PCP users: feelings of strength, power, and invulnerability.

As indicated, difficulties with speech are common. It is frequently blocked, sparse, and purposeless. Auditory and sometimes visual hallucinations may occur, more frequently at higher doses, and feelings of severe anxiety, impending doom or death may appear and disappear. Touch and pain sensations, as might be expected since PCP was originally developed as an anesthetic, are dulled and, as a result, even severe injuries sometimes occur with the user unaware or only minimally aware of their occurrence. Bizarre behavior of many types has been reported.

Users typically describe the drug as stronger than marihuana ("superpot"), perhaps more comparable to LSD, but basically "in a class by itself." As with these other drugs, a few users speak of attaining distinctly new perspectives, of a more "philosophical outlook" and of seeing their lives freshly with a new sense of unity. Great variability exists in the effects from one user to the next.

MODES OF USE

The novice user is often introduced to the drug openly or covertly by smoking it sprinkled on such leafy materials as tobacco, marihuana, or dried parsley in a "joint" (a hand rolled cigarette). Occasionally a manufactured mentholated cigarette is dipped in liquid PCP and later smoked ("superkools"). Although other routes of ingestion are sometimes used (e.g., snorting, oral ingestion, or more rarely, intravenous injection), the effects of the differing routes are similar, differing primarily in rapidity of onset of effects (as previously indicated, overdoses may be more likely with oral doses because of the longer latency period before the drug has an effect and the lessened ability to "self-titrate" the dose). In typical use, the "high" from a single dose lasts from four to six hours with an even longer "coming down" period. Both animal data (cf. Balster and Chait, this volume) and human reports suggest that a degree of tolerance develops, with increasing doses being required at the end of a "run" to achieve the same effects as at the beginning. PCP is a social drug in the sense that virtually all users report taking it in groups rather than as a solitary experience.

Chronic users are reported (Lerner and Burns, this volume) to take the drug in "runs" that may extend over two or three days during which they remain sleepless. Appetite is also reportedly suppressed, resulting in weight losses of ten to thirty-five pounds during repeated periods of chronic use. Following a "run" users need great amounts of sleep and may awaken feeling disoriented and depressed. In later stages of chronic use, outright paranoid and violent behavior with auditory hallucinations may appear.

The possible role of PCP in precipitating long term psychosis is at present poorly understood. It may be that persistent psychosis occurs in individuals who are latently schizophrenic as a result of some "triggering" function of phencyclidine. Whatever the cause, there is some evidence that individuals who have used PCP in the past may later develop a more persistent schizophrenia despite some months of abstinence from the drug (cf. Luisada, this volume).

Having used phencyclidine repeatedly without serious adverse effects is apparently no guarantee that more serious consequences will not occur unexpectedly on another occasion of use. At least one group of clinical investigators (Burns and Lerner, 1978) believes that if use is persistent, adverse consequences will almost invariably follow.

The premorbid personalities of PCP abusers are not consistently described in the literature. PCP users appear to have a variety of personalities, not fitting a single pattern. Fauman and Fauman (1977) made the point that many of those who become psychotic with this drug appear to resemble persons who become psychotic using LSD. However, PCP abusers include not only socially marginal people, but also people of substantial achievement without obvious premorbid psychopathology.

For chronic PCP users, PCP is in fact a drug of choice. Lerner and Bums (this volume) report that chronic phencyclidine users experienced persistent cognitive and memory problems. Speech difficulties included stuttering, poor speech articulation, and difficulties in expressing themselves to others, effects lasting 6 months to a year following prolonged daily PCP use. Mood disorders also occurred; viz: depression, anxiety, and violent behavior. Purposive activity became more difficult with resultant loss of employment or impaired school performance.

TREATMENT OF CHRONIC PCP USER

As with other drug abuse, the motivations of the user are crucially important in the approach to treatment. In at least one geographic area of high PCP abuse, a downturn in emergency cases, possibly indicating less widespread general use, followed an intensive effort by the local community mental health center to publicize the adverse effects of the drug. Unfortunately, numerous case accounts suggest that the user who consistently enjoys PCP will be reluctant to give up its use, since it is relatively cheap, easily available, and quite powerful. Although for many it is a particularly disagreeable drug, for others it is quite enjoyable. Whether this reflects a psychopharmacologic difference between these groups is not known, but its genuine appeal to some must be taken into account in any therapeutic or educational program. Not only is the drug readily available, but so is the example of users who experience severe depression while taking the drug, but who continue their use of it notwithstanding.

In their discussion of long term residential treatment of adolescent PCP abusers, DeAngelis and Goldstein (this volume) emphasize the importance of dealing with underlying emotional conflicts in their clients rather than focusing on their phencyclidine use itself. Discussion of drug abuse itself, they feel, is often a way in which the disturbed adolescent can avoid coming to grips with his or her real problems which cause drug abuse. In their population they have found that about half reported PCP use. They report that many of their PCP users in treatment show "flattened affect, depression, agitation, hostility, and belligerence." As a result, staff have lower initial expectations of PCP users' participation in such activities as therapy, school or recreational programs and are initially more tolerant of angry outbursts. Chronic PCP users were found to stay in the program longer than other types of drug abusers (DeAngelis and Goldstein, this volume).

PCP OVERDOSE (cf. Done, Aronow and Miceli; Aronow, Miceli and Done; Luisada; Smith et al. - all in this volume)

Diagnosis

The victim of an overdose of PCP may exhibit many different symptoms during the course of his intoxication, depending on the dose, how recently it has been ingested, and frequency of prior use. Some cardinal signs of PCP overdose are: ataxia, vertical and horizontal nystagmus, assaultiveness or catatonic staring, and generalized anesthesia. Severe convulsions may also occur in extremely heavy overdoses, and PCP exhibits the lethal properties of a central nervous system depressant, with respiratory depression, coma and death.

The dose of PCP which may result in a trip to an emergency room is as varied as the presenting symptoms. A single cigarette may, in the inexperienced (or deceived) user, produce overwhelming feelings of acute anxiety requiring prompt but relatively brief reassurance and therapeutic support. In adults, quantities in excess of a half a gram have been used and it is particularly in this dose range (or higher) that life-threatening effects are likely to be manifested along with severe behavioral disturbance.

The diagnosis of PCP over-dosage is frequently missed (Fauman and Fauman 1977). Because the presenting symptoms so often closely resemble those of an acute schizophrenic episode, this is a common misdiagnosis. Aronow and Done provide a useful summary (Aronow and Done 1978) of the range of physical and psychological symptoms likely to be encountered in the emergency room situation.

At relatively low doses (on the order of 5 mg in the adult, leading to an estimated serum level of 20-30 ng/ml) they describe the patient as likely to show some of the following symptoms:

agitation and excitemnt
gross incoordination
blank stare appearance
catatonic rigidity
catalepsy
inability to speak
horizontal or vertical nystagmus
loss of response to pinprick
flushing
diaphoresis
hyperacusis

Psychologically the patient may have the following subjective responses: changes in body image, estrangement, disorganization of thought, feelings of inebriation, drowsiness and apathy. The patient may show marked negativism and hostility as well as bizarre behavior. Later, the patient may be amnesic for the drug episode.

At moderate doses (approximately 5-10 mg., leading in the adult to serum levels of 30-100 ng/ml) they list the following symptoms:

coma or stupor
eyes remain open
pupils in midposition and reactive
nystagmus
vomiting
hypersalivation
repetitive motor movements
myoclonus (shivering)
muscle rigidity on stimulation
flushing
diaphoresis
fever
decreased peripheral sensations (pain, touch, and position)

At still higher doses (over 10 mg, leading in the adult to serum levels of 100 ng/ml and higher) the authors note the following:

prolonged coma (from 12 hours to many days)
eyes closed
variable pupil size, but reactive
hypertension
opisthotonic posturing
decerebrate positioning
repetitive motor movements
muscular rigidity
convulsions (at doses of 0.5 to 1 mg/kg)
absent peripheral sensation
decreased or absent gag and corneal reflexes
diaphoresis
hypersalivation
flushing
fever

(The doses cited are rough guidelines; other investigators suggest that significantly higher doses of PCP are needed to produce each of these clinical pictures.)

If the symptoms found are suggestive of recent PCP ingestion, a urine or blood sample may reveal the presence of the drug. If a large amount has been ingested, considerable quantities of PCP will be present in urine for several days (or more). Attempts should be trade to elicit a drug history from informants, although it is quite possible that they may only know the drug under one of its street names (cf. The Material) or may not even know that the patient has taken phencyclidine if the drug has been misrepresented. Since the drug often renders the patient amnesic for the circumstances of taking it, he or she may not remember having taken it or may only recall it during a later period of recovery. A history of recent ingestion of other drugs may complicate the diagnosis and treatment. Thus the diagnosis may sometimes be established by history, sometimes by laboratory tests, by the physical and psychological course of the patient or by some combination of these.

Treatment of PCP Overdose

Life-support measures

The hospital management of the PCP overdose victim is divided into phases corresponding to the time course of action of the drug. The initial phase requires symptomatic, often intensive medical management. It includes the most acute physical effects of the drug, including the possibility of respiratory depression, convulsions, and coma. Treatment of this phase frequently requires the full life-support capabilities of a good intensive care unit. Acidification of the urine and gastric drainage (see below) will markedly hasten the excretion of PCP. Since there is no specific antagonist for PCP other treatments are symptomatic. PCP often induces hypersecretion in the pharnyx, which must be suctioned. Respiratory depression calls for external respiratory assistance. Hyperthermia can be treated with external cooling. Life-threatening consequences of rapid development of hypertension can be treated with diazoxide (Hyperstat) or hydralazine hydrochloride (Apresoline). Convulsions can be managed with IV diazepam and constant attention to maintenance of an unimpaired airway. However, some feel diazepam may prolong the course of the intoxication.

Isolation

Most clinicians advocate placing the patient in an isolated environment during this period, reducing sensory stimulation as much as possible in order to minimize the phase of excitability, irritability, anxiety, paranoia and violence which often follows the obtunded or comatose phase. Needless to say, such isolation of the patient (in quiet rooms, etc.) cannot be at the expense of vigilant medical monitoring of the patient's vital signs and his/her response to emergency life-support management. Patients are often so unmanageable that restraints are necessary, and the help of four or five (not one) burly aides will often be needed to prevent injury to staff or patients. If it is necessary to administer tranquilizing agents to keep the patient manageable, do not use phenothiazines during this acute stage because of the anti-cholinergic potentiation with PCP. Haloperidol (Haldol) has been recommended (5 mg IM repeated hourly until the patient is under control).

Detoxification

Recently ingested drugs should be removed by gastric lavage. Done (1978) and Aronow and Done (1978) describe an emergency detoxification procedure which achieves greatly enhanced urine concentrations of PCP by lowering the urine pH to 5 or less. They recommend administration of ammonium chloride by gastric intubation or, in severe cases, intravenously. (Prior screening must be done for the concomitant presence of such other drugs as phenobarbital or salicylates, whose excretion might be adversely affected by acidification; the presence of liver damage contraindicates the use of ammonium chloride.) To acidify by intubation they use 2.75 mEq/kg ammonium chloride in 60 cc or saline solution every 6 hours along with intravenous ascorbic acid (2 gm/500 cc IV fluid q 6 hours) until the urine pH drops below 5. For patients in deep coma, they advise using intravenous ammonium chloride (2.75 mEq/kg as a 1-2 percent solution in saline) with precise and repeated monitoring of blood pH, blood gases, BUN, blood ammonia levels, and electrolytes. These guidelines must be adapted for every patient individually by a medical team experienced in electrolyte management.

The treatment of acute toxic effects usually belongs in an intensive care unit, not an emergency room. Constant gastric suctioning is essential because PCP can pool in gastric contents, and should be continued well past the point of awakening from coma. The excretion of PCP is variable and prolonged. Ten days to two weeks of further acidification using cranberry juice is indicated, because of remaining body stores of PCP.

If medical treatment is successful, the patient's coma will lighten, only to be replaced, frequently, by delirium, paranoia, and violent assaultiveness. This may occur at the same time as life-support measures are still necessary, requiring constant attention from the medical staff so that intubation and intravenous lines remain open and intact. Any patient in whom coma is followed by a prolonged period of confusion should, as recommended by Burns and Lerner (1978) have a psychiatric consultation prior to discharge to evaluate residual paranoia or potentially suicidal depression.

PCP Psychosis

a. Diagnosis

Some patients experience a psychotic phase which lasts from several days to several weeks despite abstinence from further PCP. The psychosis may occur after single doses of PCP. Luisada (this volume) divides these psychoses into three stages, each lasting several days: the initial stage, characterized by violent psychotic behavior; the second stage, with restless but more controlled behavior and a lessening of delusional activity; and the final stage, characterized by rapid improvement of thought disorders and amelioration of paranoia.

It should be emphasized that this psychotic stage may be the first stage at which the patient enters treatment, often through a psychiatric hospital emergency room rather than a general medical hospital emergency service. The PCP user may at this point be misdiagnosed as schizophrenic, especially if a drug history is unavailable or inaccurate. He may or may not have passed through an earlier stage of reduced consciousness or coma in the company of friends or by himself, but presents with a psychotic-like picture of confusion, incoherent speech, paranoia, assaultiveness, restlessness, autism, preoccupation, mutism, auditory hallucinations, and grandiosity. An erroneous diagnosis of schizophrenia does not complicate his or her immediate treatment, which is much the same for acute schizophrenia, but labels him with a diagnosis which may be quite inappropriate and misleading for future medical contacts.

b. PCP psychosis - a psychiatric emergency

Phencyclidine psychosis constitutes, in this initial phase, a psychiatric emergency, one often misidentified (in St. Elizabeth's hospital in Washington, D.C., PCP psychosis actually became for two years the leading cause of inpatient psychiatric admission, outstripping both schizophrenia and alcoholism). The patients are dangerous to themselves, because of depression and suicidal impulses, and dangerous to others, because of paranoia and strong tendencies toward violence. For patients fitting this description, psychiatric inpatient treatment is indicated. Voluntary hospitalization is seldom acceptable to the hostile, suspicious patient. The immediate goals of treatment for this acute PCP-induced psychosis (Luisada, this volume) are:

1. prevention of injury to the patient or others
2. assurance of continuing treatment
3. reduction of stimuli
4. amelioration of psychosis
5. reduction of agitation

c. Treatment of PCP psychosis

In treating the psychosis, most clinicians prefer to use haloperidol, 5 mg IM given hourly if needed, to avoid the possibility of potentiation of PCP anticholinergic effects by a phenothiazine. Chlorpromazine is also effective, but prior to instituting any phenothiazine treatment of a psychotic patient with a history of PCP use, it is essential to determine whether the patient is still intoxicated with PCP. The patient should be examined for the presence of nystagmus and ataxia, which, if present, indicate intoxication. The pupils should also be examined to guard against anticholinergic drug intoxication. If there is no possibility of continuing intoxication by a cholinergic drug, chlopromazine may be given instead, starting with 400 mg/day orally in divided doses (after a test dose of 50 mg) and increased as necessary by 200-600 mg/day. On the average, a daily dose of 1600 mg/day of chlorpromazine will be reached by the end of the initial phase of treatment. The response of PCP psychosis to this aggressive treatment is characteristically slow, distinguishing it from paranoid schizophrenia, which usually responds much more rapidly.

As the psychotic symptomatology abates, there are sometimes unpredictable reexacerbations. Patients will often wish to sign out against medical advice, with encouragement from others to do so, only to experience unexpected suicidal or homicidal impulses following their discharge (the patient may still not realize, because of drug-induced amnesia, that PCP was responsible for his hospitalization). When feasible, group and milieu psychotherapy can help.

Outpatient follow-q treatment is aimed at keeping the patient away from resuming drug use, a task which is not always easy despite the dysphoria associated with the experience which led to hospitalization. Luisada and Brown (1976) make the provocative observation that “about one-fourth of the patients originally treated for phencyclidine psychoses return about a year later with schizophrenic ones in the absence of drug use. . . These later episodes have lacked the characteristic violence of the phencyclidine-induced ones, and they have been much more quickly responsive to antipsychotic drugs.” Thus, some of the users who became psychotic under PCP may have been “at risk” for schizophrenia, which later reappeared without the precipitating drug. (Some, in fact, may have been identifiably schizophrenic prior to using the drug.)

Profound depression is experienced by significant numbers of users (not just overdose cases). They must be followed carefully to monitor their suicidal potential (Smith et al. 1978).

PHENCYCLIDINE -- THE UNANSWERED QUESTIONS

Our present knowledge of phencyclidine as an abused drug is decidedly modest. Indeed, as was pointed out earlier in this account, even the basic data pertaining to the incidence and prevalence of its abuse are largely lacking. What information is available represents a minimal estimate of both the extent of PCP use and of possible adverse effects of such use. Since PCP is often misrepresented as some other drug, inquiring about its use is certain to represent an underestimate of such use, especially by the less chronic user. And, as we have seen, the individual who suffers from a schizophrenic-like reaction to the drug is likely to be diagnosed as an acute schizophrenic reaction rather than as a toxic drug reaction.

Our understanding of the personality characteristics of more chronic users and the effect that phencyclidine has on their lives is also limited. For example, there is some question whether or not the acute schizophreniform reaction sometimes encountered in users may not be indicative of a latent schizophrenia precipitated by the drug. Similarly, we know little of the frequency and circumstances under which PCP potentiates aggression, although there have been many individual clinical reports of highly destructive behavior related to drug use.

Although it is believed that PCP ultimately results in "burned out," dulled intellectual functioning after repeated use, this has yet to be verified objectively. Besides possible adverse effects on intellectual functioning, phencyclidine may also disrupt psycho-social functioning in ways that remain to be delineated. Because it is widely used during adolescence, it is especially important to assess its possible effects at this age.

A still puzzling paradox not yet fully explained is the apparent increase in PCP use in recent years despite a continued poor street reputation of the drug. This increased popularity may reflect the improved ability of the user to avoid overdose when the drug is smoked or snorted rather than taken orally, the desirability of simply changing one's state (Cf. Mello, this volume), the marked increase in PCP availability or some combination of these and possibly other factors as well. Despite speculation, the motives for use of phencyclidine remain poorly understood.

Lasting biological implications of use and especially of chronic use arc largely unknown. These include possible reproductive effects of PCP use as well as possible alterations in neurophysiological functioning that may be related to prolonged use. While higher doses of this drug are unquestionably incapacitating, much less is known about the effects of lower doses which may be more typical of recreational use, especially when the drug is smoked. Thus the wide range of possible dose response relationships involving PCP needs elucidation. Carefully designed experiments which investigate the relationships between dose, tissue and fluid levels, and pharmacological and behavioral effects of PCP and its analogs should be conducted in man where medically and ethically possible. Since PCP is often used in association with such other drugs as alcohol, marihuana, and the barbiturates, it is important to know the effects of such combinations. For example, doses of alcohol or PCP which are not seriously toxic alone may become so when both drugs are taken concomitantly.

Similarities and differences between PCP and other abused substances can be evaluated in animals with sensitive behavioral techniques. Behavioral and drug-specific variables which contribute to the initiation and maintenance of PCP self-administration should be studied. The effects of PCP on a wide range of behaviors (e.g., aggression, punishment- induced conflict, cognitive function and sensory discrimination) remain to be investigated. The long term behavioral- toxicological consequences of phencyclidine administration should be examined in these contexts.

Unfortunately , phencyclidine has about 30 analogs -- drugs with slightly different chemical structures which nevertheless have similar effects. Little is known about the similarities or possible differences in effects between these compounds and PCP.

Recent attention to the detection and quantification of phencyclidine in biologic samples has provided valuable techniques, which are based on standard and existing methods. These must be made readily available for clinical and research purposes. There is considerable need for detailed information on the metabolism, disposition, and pharmacokinetics of phencyclicline and its analogs in acute and chronic situations. This must in turn be matched with carefully gathered clinical data and used to improve treatment methods for overdoses.

Finally it is important that we develop effective prevention strategies to discourage PCP use. In the past, some success has been obtained in discouraging the use of other drugs by making widely known their harmful effects. Unfortunately this approach would not seem to work with PCP. The dangers of its use -- both short and long term -- are apparently quite well known to its users. We will have to understand the reasons for its use and the most effective ways to reach and dissuade the user. These goals become particularly important for a drug, or family of drugs, whose street availability cannot be substantially diminished by means presently known.

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Chapter 2

Neurobiology of Phencyclidine–An Update

Edward F. Domino, M.D.

INTRODUCTION

About 22 years aqo I was on a plane flying from San Francisco to Detroit. On the same plane was Dr. A.C. Bratton, at that time the Director of Pharmacological Research at Parke Davis Laboratories in Detroit. It took about six hours to fly across the country so we had much to talk about but especially about a fascinating compound that they had just discovered (Chen et al. 1959). Dr. Bratton said that in rodents it was amphetamine-like but it also made them drunk and ataxic. In dogs the chemical caused yelping and convulsions. Monkeys were beautifully "tranquilized" and in larger doses anesthetized by this agent. The Parke-Davis research staff was confused. They really did not know what to do with this compound. They were wondering whether they should take it into man or drop it. Would I be interested in taking a look at it? My response was positive and we did take a preliminary look at the compound. Our initial studies were in the Macaca mulatta monkey. In this species the agent was remarkable! It caused serenity, hence the trade names Sernyl or Sernylan. As far as I was concerned, it was the best anesthetic agent I had ever seen for the monkey. It appeared to be very safe compared to other general anesthetics. So remarkable was this state of anesthesia that a decision was made to file this new drug, whose code number was CI-395 and which was subsequently called phencyclidine, with the Food and Drug administration. Greifenstein, in Anesthesiology at Detroit General Hospital and Wayne State University, was asked to test it as a general anesthetic in patients. This he did (Greifenstein et al. 1958). He was so amazed at the remarkable anesthetic state it induced that with Meyer in Neurology at Wayne State University, he concluded that phencyclidine produced sensory deprivation (Meyer, Greifenstein and De Vault 1959). At that time Luby, also from Wayne State, was studying sensory deprivation as a model of schizophrenia at the Lafayette Clinic. After he heard about phencyclidine, he decided to compare it to actual sensory deprivation in both normals and schizophrenic patients (Luby et al. 1959). Luby was so impressed with the findings that he recommended to Jacques Gottlieb, then Director of the Lafayette Clinic, that I be asked to be their pharmacological consultant, for he knew that I had done some of the animal studies with this drug. So began my clinical introduction to phencyclidine and a long and fruitful association with the Lafayette Clinic.

In 1964, when we reviewed the neurobiology of phencyclidine (Domino 1964) it impressed us that the development of a new drug provides the pharmacologist and clinician with a number of surprises. That conclusion is even more true today. Who would, in their wildest imagination, predict that a dissociative anesthetic, which produced a high incidence of anesthetic emergence phenanena and was adrugwhichmimicked the primary symptoms of schizophrenia by distorting body image, would become the number one drug of abuse in the United States in 1978? Yet that is what the drug culture of our country has acomplished with phencyclidine. Surely a schizophrenomimetic drug in low dosage, and anesthetic and a convulsant in large doses, would not seem to be reinforcing - yet it apparently is to many people who now call it by many different names, including PCP, synthetic THC, angel dust, hog, crystal, animal tranquilizer, horse tranquilizer, peace pill, Pea Ce Pill, crystal joint, CJ, KJ, sheet, and rocket fuel. People who abuse phencyclidine have been called parsley monsters when the drug is applied to parsley and smoked. Those who are "high" on phencyclidine are said to be "crystalized." The drug is taken by inhalation, orally, intranasally (snorted), and intravenously. Knowing what we now know, would any of us who were involved with the early pharmacological birth and development of phencyclidine have ventured further? What have we thought?

Depending on the dose and species, phencyclidine is a excitant or a cataleptoid anesthetic. While it is an anesthetic in man, small doses cause a rather remarkable psychotomimetic picture. Emergence delirium is often seen. Phencyclidine and related compounds have been called cataleptoid and or sympathomimetic anesthetics. During induction the patient often feels dissociated from his environment with analgesia and some amnesia.

A related congener of phencyclidine is ketamine, a valuable anesthetic agent used therapeutically throughout the world. Its anesthetic properties in humans were first described as representing a new class of "dissociative" anesthetics because of its unique pharmacological actions (Domino, Chodoff, and Corssen 1965; Corssen and Domino 1966). During anesthesia, the patient may keep his eyes open and seems "disconnected" from the environment. It seems as if higher associational functions of the brain are markedly depressed, a clinical impression for which there is some human and animal physiologic data (Corssen, Miyaska, and Domino 1968; Miyasaka and Domino 1968; Corssen, Domino, and Bree 1969; Winters 1972). During emergence from dissociative anesthesia, the patient may go through a phase of vivid dreaming with and without psychomotor activity, manifested by confusion and irrational behavior.

Chemically, phencyclidine, ketamine and related compounds are arylcyclohexylamines. While they have somewhat similar pharmacological actions, they also have important differences,both quantitatively and qualitatively. The major pharmacological properties of these agents can be summarized as follows:

1. Central nervous systan
    a. Small doses produce a "drunken" state with numbness of the extremities; saw species are excited.
    b. Moderate doses are analgesic and anesthetic.
    C. The psychic state crudely resembles sensory isolation, except that sensory impulses, if tested electrophysiologically, reach the neocortex but the neuronal signals are grossly distorted.
    d. Cataleptoid motor phenomena are seen.
    e. barge doses may produce convulsions. This is especially true of phencyclidine.
    f. Marked species differences are present. Primates,especially man, are most susceptible to the depressant effects which predominate.
2. Autonomic and cardiovascular system
    a. Sympathomimetic.
    b. Tachycardia.
    C. Hypertension.
    d. Potentiation of catecholmines through a cocaine-like action.

CYCLOHEXYLAMINES ABUSED

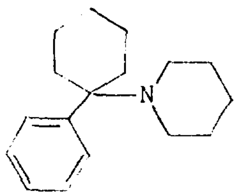
To date, at leasts six cyclohexylamines have been either given to or taken by humans in the context of drug abuse. Their chemical structures are shown in figure 1.

Kalir et al. (1969) have provided us with the best structure-activity studies of these compounds to date. Shulgin and MacLean (1976) have described the illicit synthesis of phencyclidine and several of its analogs as well as relative potency data of compounds now available on the street.

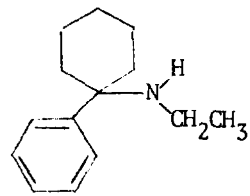
As described above, the first arylcyclohexylamine studied in man as a general anesthetic was phencyclidine (Greifenstein et al. 1958). It is longer acting and has stimulant and convulsant prop erties in man. Ketamine (Ketalar, Ketaject) has more depressant properties than phencyclidine and is shorter acting. It is used as a nonbarbiturate anesthetic in man. When phencyclidine is taken by humans, it produces more emergence delirium, in which some patients show post anesthetic psychiatric complications for as long as two weeks after a single dose. Although phencyclidine is no longer used as a general anesthetic in man, it is still a veryusefulanesthetic in veterinary medicine, especially for primates (Domino, McCarthy, Deneau 1969).

Widespread use of phencyclidine as a psychedelic agent by the drug subculture in the United States is now generally acknowledged. The early warning drug network (DAWN) has emphasized that phencyclidine has been a major drug abuse problem for same time. One

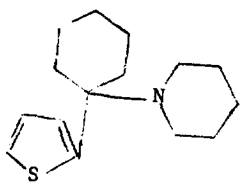
FIGURE 1



Phencyclidine (PCP)
1-(phenylcyclohexyl)
piperidine (CI-395)

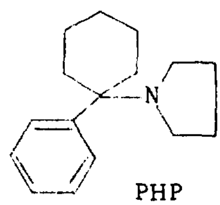


Cyclohexamine (PCE)
N-ethyl-1-phenylcyclohexylamine
(CI-400)



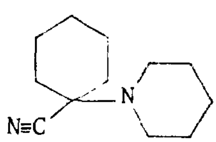
TCP

1-(1-2-thienylcyclohexyl)
piperidine

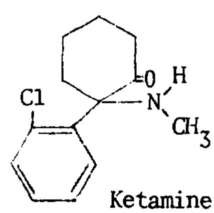


PHP

1-(1-phenylcyclohexyl)
pyrrolidine



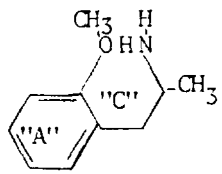
PCC
1-piperidinocyclohexane-
carbonitrile



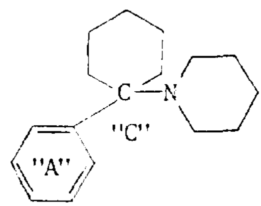
Ketamine
2-(o-chlorophenyl)-2-methyl-
amine cyclohexanone (CI-581)

of the clinical problems associated with phencyclidine overdosage is that the patients not only may be in coma but they may also convulse and die of respiratory arrest. The prolonged emergence delirium is observed in patients who may be psychotic for at least several weeks or more. This may be due to metabolic or psychiatric variables such as pre-morbid or borderline schizophrenia. The clinical toxicology of phencyclidine is of such importance that an entire issue of Clinical Toxicology in August of 1976 was devoted to it (Burns and Lerner, Guest Editors, 1976).

If one has a vivid imagination, there is a structural relationship between phencyclidine, amphetamines and LSD-25. I have drawn 2-methoxyamphetamine and phencyclidine to approximate the A and C rings of LSD-25 as shown below:



2-Methoxyamphetamine



Phencyclidine

NEUROCHEMISTRY

The most recent review of the neurochemical pharmacology of phencyclidine is by Johnson in this monograph. Our own interests in this area may provide an additional point of view and will be an update of our own brief review (Domino and Luby 1973).

A. Monoamines, Especially Catecholamines and Serotonin.

Because of the structural similarities, one would expect phencyclidine to interact with the monoamines in the body, especially the catecholamines (CA) and 5-hydroxytryptamine (5-HT). Chen and his associates (1959) compared the sympathomimetic effects of phencyclidine with cocaine and desoxyephedrine. They concluded that it had similarities to both drugs, especially cocaine. O'Donnell and Wanstall (1968) studied the action of phencyclidine on the perfused rabbit ear. They postulated that phencyclidine inhibited the uptake of both norepinephrine (NE) and tyramine by adrenergic neurons in a manner similar to that of cocaine. High concentrations of phencyclidine (Ki = 1.5 x 10^{-4}M), like many other psychotropic drugs, inhibit monoamine oxidase (MAO) activity but this does not appear to be significant in relation to its in vivo actions (Usdin and Usdin 1961).

The effects of phencyclidine on the pressor responses to norepinephrine (NE), epinephrine (EPI), and serotonin (5-HT) in the pentobarbital-anesthetizeddog are consistent with a cocaine-like action as illustrated in figure 2 below.

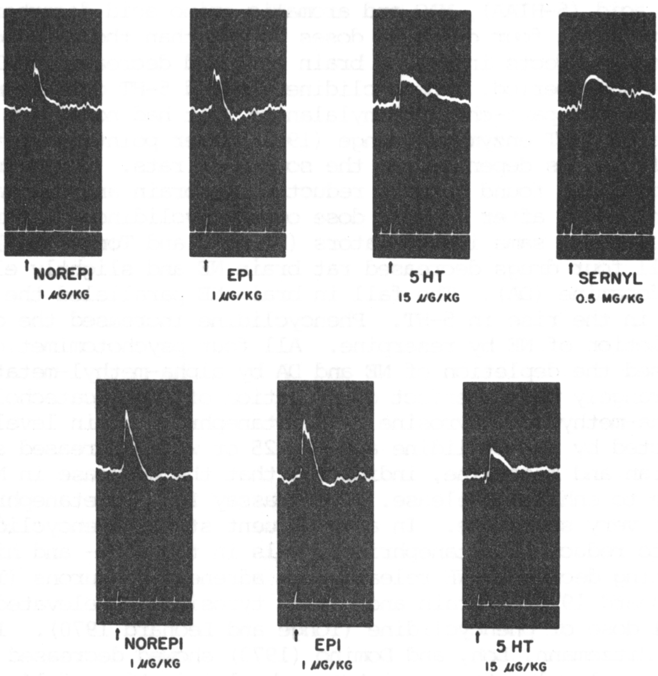
Note that 0.5 mg/kg of i.v. phencyclidine itself produces an initial transient hypertensive response which is probably related to peripheral CA release. Ketamine produces a similar hypertensive response but apparently has less of a cocaine-like potentiating action than phencyclidine.

Tonge and Leonard (1969) compared the effects of phencyclidine, Ditran, mescaline and LSD-25 on rat brain 5-HT, 5-hydroxyindole-acetic acid (5-HIAA), MAO and aromatic amino acid decarboxylase activity. All four drugs in doses larger than those heeded for behavioral effects increased brain 5-HT and decreased 5-HIAA over a three hour period. Phencyclidine reduced 5-HT depletion after reserpine and para-chlorophenylalanine. It had no effect on the associated 5-HT enzymes. Tonge (1971) later pointed out that this effect was dependent on the source of rats. Tonge and Leonard (1970) found a small reduction in brain and plasma tryptophan levels after a small dose of phencyclidine. A parallel study of these same investigators (Leonard and Tonge 1969) showed that all four drugs decreased rat brain NE and slightly elevated brain dopamine (DA). The fall in brain NE paralleled the time course in the rise in 5-HT. Phencyclidine increased the degree of depletion of NE by reserpine. All four psychototmimetic agents increased the depletion of NE and DA by alpha-methyl-metatyrosine, but strangely had no effect on depletion of these catecholamines by alpha-methyl-paratyrosine. Normetanephrine brain levels were unaffected by phencyclidine and LSD-25 or were decreased slightly by Ditran and mescaline, indicating that the decrease in NE was not due to enhanced release. Their assay for normetanephrine was not very sensitive. In a subsequent study, phencyclidine was shown to reduce normetanephrine levels in the fore- and hindbrain, indicating decreased NE release from adrenergic neurons (Tonge and Leonard 1972). Brain and plasma tyrosine are elevated after a small dose of phencyclidine (Tonge and Leonard 1970). In the mouse, Hitzemann, Loh, and Domino (1973) showed decreased $14_{C\text{-}NE}$ and $14_{C\text{-}DA}$ levels after an intracerebral injection of 14_C-tyrosine after phencyclidine. An increase in $14_{C\text{-}3}$-methoxytyramine and 14_C-normetanephrine was noted. In the mouse striatum phencyclidine does not significantly change homovanillic acid levels (Sharman 1966).

Sung, Frederickson, and Holtzman (1973) have shown that 40 mg/kg of ketamime increased the turnover of DA and decreased the turnover of 5-HT in rat brain four to six hours postinjection, although the behavioral effects lasted only two to three hours. The cocaine-like actions of phencyclidine have also been reported for ketamine. Miletich et al. (1973) have shown that ketamine prevents the neuronal reuptake of NE in rat heart.

Leonard and Tonge (1968, 1970) looked at other putative neurotransmitters in the rat brain following phencyclidine. They found no changes in whole brain acetylcholine, cholinesterase and

FIGURE 2



Effects of phencyclidine on the arterial blood pressure responses of norepinephrine, epinephrine, serotonin in the pentobarbital anesthetized dog.

Each agent was given us a bolus i.v. injection at 5-10 minute intervals. Note the cocaine-like action of phencyclidine to enhance the pressor responses of the CA in contrast to 5-HT where the effects are more variable.

histamine. However, a high dose of phencyclidine decreased brain GABA They also found an increase in 5-hydroxytryptamine decarboxylase activity. In a preliminary study, Tonge (1973) found that chronic phencyclidine during the pre- and post-neonatal periods produced elevated 5-HT levels in the rat hypothalamus and pons-medulla.

B. Acetylcholine

There have not been enough studies on the complex effects of the arylcyclohexylamines on the cholinergic system. In vitro phencyclidine (5×10^{-5}M) inhibits primate serum cholinesterase using benzoylcholine as substrate (Becker 1969). In humans, the usual and fluoride variants of serum cholinesterase are inhibited by phencyclidine whereas the dibucaine variant shows increased resistance. This differential inhibition suggests that phencyclidine is useful in estimating human genotypes for cholinesterase. Apparently, phencyclidine and acetylcholine have similar charge distributions in relation to muscarinic cholinergic receptors (Weinstein et al. 1973; Paster et al. 1974; Maayani et al. 1974). This would account for phencyclidine having an atropine-like effect. However, phencyclidine not only inhibits serum or butyrylcholinesterase, it also inhibits acetylcholinesterase with a larger Ki (about 80 times greater). These mixed agonist and antagonist actions of phencyclidine tend to antagonize each other. However, the algebraic sum of the actions of phencyclidine on guinea pig ileum is predominantly antagonistic (Maayani et al. 1974). Amazingly, in mice, scopolamine has been reported to prevent tolerance develop ment to cyclohexamine (Pinchasi, Maayani and Sokolovsky 1977). Ketamine is also reported to inhibit both serum butyrylcholinesterase (Schuh 1975) and brain acetylcholinesterase (Cohen et al. 1974). Although in large doses phencyclidine has been reported to elevate slightly brain ACh (Giarman and Pepeu 1962), Leonard and Tonge (1968, 1970) and Domino and Wilson (1972) have shown that smaller but behaviorally effective doses do not alter total ACh levels. Phencyclidine also increases the depletion of rat brain ACh after hemicholinium-3, suggesting an increased utilization of ACh in smaller doses. Like LSD-25, phencyclidine does not significantly alter the release of ACh fran the cat cerebral cortex in contrast to the isomers of Ditran, which increase ACh release, and general anesthetics like pentobarbital which decrease ACh release (Domino and Bartolini (1972). Ngai, Cheney and Finck (1978) measured regional ACh and Ch concentrations in the brains of rats given halothane, enflurane and ketamine as well as the turnover rate of ACh in vivo. ACh concentrations in various brain areas did not change during anesthesia with any of the anesthetics studied. This is noteworthy in itself because ketamine in vitro is a cholinesterase inhibitor (see above). Yet in vivo steady state levels of ACh were not elevated, as would be expected. During anesthesia with ketamine, ACh turnover rates were reduced in the caudate nucleus and hippocampus, but not in the cerebral cortex, thalamus and hypothalamus. Halothane decreased ACh turnover in all of the brain regions while enflurane only decreased ACh turnover in the cortex. These investigators felt that the changes in ACh turnover were related to known anesthetic-induced electrophysiologic changes in cortical and subcortical structures.

C. Energy production

Phencyclidine has still other effects on the enzymes involved with energy production. *In vitro* phencyclidine (5×10^{-4}M) is an uncoupler of oxidative phosphorylation (Lees 1962, 1968). The drug *in vitro* increased rat liver mitochondrial respiration in low concentrations and depressed it in high concentrations. ATPase activity was stimulated and the inorganic phosphate-ATP exchange reaction inhibited. These in vitro effects of phencyclidine onrespiration, ATPase activity,and the inorganic phosphate-ATP exchange reaction were crudely similar to-those of chlorpromazine except higher concentrations of phencyclidine were required. Only in even greater concentrations was the drug inhibitory.

NEUROPHYSIOLOGY

It is clear that phencyclidine produces its own unique EEG; changes in nomal humans. Van Meter, Owens and Hinwich (1960) using rabbits provided evidence that phencyclidine acts on the cerebral cortex. Our own studies (Domino 1964; Miyasaka and Domino 1968) also implicate a thalamo-cortical action of phencyclidine and its congener, ketamine. Adey and Dunlop (1960) have pointed out that phencyclidine and cyclohexamine in cats suppresses or seriously interferes with learned approach in a T-maze situation. This was correlated with EEG; spikes and abolition of normal hippocampal activity. After these drugs stimulation of the thalmic nucleus ventralis anterior failed to elicit nomal hippocamal theta wave activity. Drug-induced changes in the reticulo-cortical system were also seen, but the hippocampal changes were especially apparent. Winters et al. (1967) compared the EEG; effects of phencyclidine in cats with other general anesthetics. They suggested that hallucinatory and epileptoid phenomena as well as general anesthesia were in part a continuum with reticular, thalamic, cortical and hippocampal alterations, depending upon the class of drugs studied. Winters and Ferrar-Allado (1972) showed that ketamine induced a catatonic state in cats which was accompanied by intermittent or continuous hypersynchronous discharges from the cortex, limbic structures and the medial geniculate nucleus. An especially provocative viewpoint was expressed by Winters (1972) When he suggested ketamine was causing epilepsy instead of anesthesia in man. This point of view has been criticized by Corssen, Little, and Tavakoli (1974) and Domino (1974). Nevertheless, Winters and his colleagues have documented extensively the stimulant and convulsive properties of both phencyclidine and ketamine, especially in animals. There is no question that given enough of each of these substances in an appropriate species, convulsions are seen. This is well documented in human overdosage With phencyclidine in particular. The extensive studies of Winters as well as a review of the literature on the neuropharmacology of anesthetics were recently summarized by him (Winters 1976).

Phencyclidine effects on the EEG; of chronic schizophrenics, both lobotomized and not, were studied by Itil et al. (1967). While the two groups showed symptoms to 0.05 mg/kg of phencyclidine given over a 5 minute period, the lobotomized patients showed much less alteration to both clinical symptoms and the alpha frequency decrease in the EEG. These investigators concluded that the inability of lobotomized patients to exhibit marked phencyclidine effectsin comparison to the nonlobotamized patients was because thalamcortical integrative mechanisms are necessary to produce typical phencyclidine responses. Fink (1969) reviewed the effects of phencyclidine along with many other psychoactive compounds on the human EEG. Stockard et al. (1975) have reported that the unusual delta wave activity followed by low voltage fast wave activity we have previously reported in the monkey was observed in a 25 year old male patient who inhaled a rather large amount of "angel dust." His serum phencyclidine levels were reported as being 0.34 µg/ml. These investigators reported similar EEG; changes due to 2 to 4 mg/kg of ketamine given intravenously. They suggested that these EEG manifestations of diffuse monorhythmic theta activity with superimposed periodic events should raise the suspicion of cyclohexylamine intoxication in comas of unknown etiology. It is not known if the other cyclohexylamines besides phencyclidine and ketamine produce similar EEG manifestations and whether these are correlated with plasma levels.

BEHAVIORAL STUDIES

The meager animal and human behavioral studies available until a few years ago were reviewed by us previously (Domino 1964; Domino and Luby 1973). Since then, the behavioral pharmacology of phencyclidine has been reviewed by Balster and Chait (1976) and again very recently (Balster and Chait, this monograph). Especially important is the evidence that both phencyclidine (Balster and Johanson 1973; Pickens, Thanpson and Muchow 1973) and ketamine (Moreton et al. 1977) are self-administered by animals. In addition, drug discrimination studies indicate that phencyclidine, cyclohexamine, and ketamine belong to a class of their own for they do not transfer stimulus control to morphine, chloropromazine, Ditran, Δ^9-tetrahydrocannabinol or pentobarbital. It is especially important to know whether in low dosage there is stimulus generalization of phencyclidine to cocaine and amphetamine-like drugs and in larger dosage to general anesthetics including nitrous oxide, halothane and convulsants like phentylenetetrazol. Whether the technical behavioral problems can be solved remains to be seen.

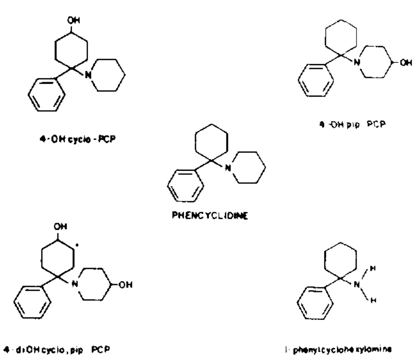
One extensive locomotor activity study using 5 mg/kg i.p. of phencyclidine has been reported by Kanner et al. (1975). It was previously known that phencyclidine produces increased locomotor activity in mice which can be augmented by pretreatment with iproniazide (Chen et al. 1959). Phencyclidine also enhances motor activity in rats. Kanner et al. found that pretreatment with alpha-methyl-paratyrosine (250 mg/kg, i.p.) decreased phencyclidine-elicited activity by 43 percent ($p < .05$) in one hour. Iproniazid (100 mg/kg, i.p.) increased phencyclidine-elicited activity by 61 percent. Pretreatment with phenoxybenzamine (10 mg/kg, i.p.) decreased phencyclidine-elicited activity by 85 percent ($p < .05$) while pretreatment with propranolol (25 mg/kg, i.p.) increased phencyclidine-elicited activity by 56 percent ($p < .05$). Pimozide (1 mg/kg, i.p.) decreased phencyclidine-elicited activity by 57 percent ($p < .05$) while haloperidol (0.5 mg/kg) decreased phencyclidine-elicited activity by 90 percent ($p < .05$). Trihexyphenidyl (5 mg/kg, i.p.) and atropine (10 mg/kg, i.p.) significantly increased phencyclidine-elicited activity by 93 percent and 43 percent, respectively, while arewline (10 mg/kg, i.p.) and physostigmine (0.4 mg/kg, i.p.) decreased phencyclidine-elicited activity by 23 percent and 61 percent, respectively. Their data indicate that the stimulation of locmotor activity produced by phencyclidine can be influenced by noradrenergic, dopaminergic, and cholinergic inputs. The major criticism of this kind of research is that most agonists and antagonists are known to alter rat locomotor activity. Hence, interpretation of such findings is must difficult and probably not very rewarding fran a therapeutic point of view.

Perhaps the most important behavioral study that must be done is to answer the question, why do animals and people take these drugs? Why is it reinforcing to mimic the primary symptoms of schizophrenia, to be in coma, convulse, and maybe die from overdosage? I cannot imagine that being a "parsley monster" or being "crystalized" is really very wonderful.

BIOTRANSF0RMATION AND PHARMACOLOGICAL ACTIVITY OF METABOLITES

The biotransformation of phencyclidine is just beginning to be understood. Some of the proposed matabolites of phencyclidine are shown in figure 3 below.

FIGURE 3

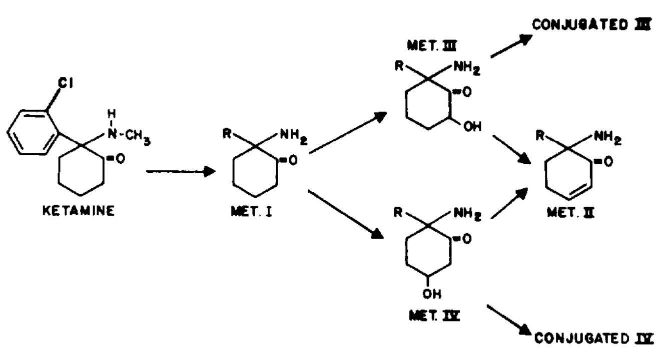


Some Metabolites of Phencyclidine

Lin et al. (1975) have described some of the metabolities of phencyclidine they found in urine of intoxicated human patients. Two conjugated hydroxylated compounds were found. These were 1-(1-phenyl-4-hydroxycyclohexyl)-piperidine (4-OH cyclo PCP) and 1-(1-phencyl-cyclohexyl)-4-hydroxylpiperidine (4-OH pip PCP). In addition, a dihydroxylated metabolite tentatively identified as 1-(1-phencyl-4-hydroxy-cyclohexyl)-4-hydroxy piperidine has been found in monkey urine. Wong and Biemann (1975) have reported that 1-phenycyclohexylamine is also a metabolite of phencyclidine in man and mouse. The findings of Lin et al. are in partial agreement with those of Ober et al. (1963), who reported that monkeys excrete mainly the dihydroxy metabolite. In their preliminary report, they stated that the dihydroxy metabolite did not have any phencyclidine activity. Our own studies (Domino 1978) indicate that both 4-OH cyclo PCP and 4-OH pip PCP have biologic activity in both the rat and dog. one would expect the hydroxylated derivatives of phencyclidine to be more water soluble and to penetrate the blood-brain barrier less. Although these compounds are less potent than phencyclidine, they apparently cross the blood-brain barrier in sufficient amounts, for they have important convulsant components. Hence they may play a role in phencyclidine overdosage in man. Much more work is obviously needed to determine not only the detailed biotransformation of phencyclidine but also the pharmacological properties of its metabolites.

The biotransformation of ketamine is also imcompetely understood. The scheme proposed by Chang and Glazko (1974) is given in figure 4.

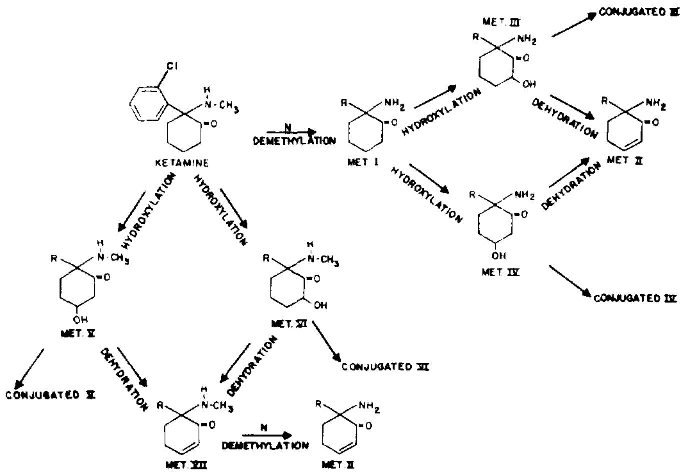
FIGURE 4



Biotransformation Pathway of Ketamine, proposed by Chang and Glazko 1974

Our own proposed scheme is based on that of Chang and Glazko (1974) but introduces a further order of complexity, as shown in figure 5.

FIGURE 5



One should realize how meager is our knowledge of the pharmacology of each of these proposed metabolites. In most cases, they need to be synthesized and studied further.

CHEMICAL ANALYSIS

Phencyclidine has been analyzed chemically from biological samples using both qualitative and quantitative techniques. Thin layer chromatography, gas chromatography, and gas chromatography-mass spectrometry and radioimmunoassays have been used. Hawks and Willette (1977) briefly reviewed these methods with the exception of the radioimmunoassay procedure developed by Kalir et al. (1976). The latter seems very pranising but unfortunately, has not attracted any interest in the United States to date.

From a practical point of view, the most available quantitative procedures in the United States at this time involve gas chromatography using a flame ionization detector or combined gas chromatography-mass spectrometry using either electron impact or chemical ionization. Reynolds (1976) and Marshman, Ramsay, and Sellers (1976) have employed gas chromatographic techniques for the quantitative assay of phencyclidine from urine, tissues, and plasma. Reynolds used ether extraction of the urine with OV-1 and OV-17 GLG columns at a temperature of 180°C. The tissue and blood samples were prepared with 0.5 N HCl. Mepivicaine was used as the internal standard. After strong alkalization, phencyclidine was extracted with chloroform and assayed as above. Marshman, Ramsay, and Sellers used a similar assay except that ketamine was the internal standard. In addition, 3.8 percent UCW-98 on Gas Chrom Q at a temperature of 200° C was used. Gupta et al. (1975) used methadone as the internal standard for phencyclidine in human urine using Chromasorb W coated with Apiezon L at 200°C. Finkle's gas chromatographic method (quoted by Hawks and Willette 1977) uses SKF 525A as the internal standard using a 3 percent OV-1 or OV-17 with a column temperature of 130-270°C. It should be noted that these investigators all used column and/or injection port temperatures of 200°C or above. We know now that phencyclidine undergoes thermal decomposition to 1-phenylcyclohexene at temperatures above 150°C (Lin et al. 1975; Wong and Biemann 1975, 1976). These investigators recommend temperatures below 200°C for quantitative purposes.

Obviously, the most specific assays involve the use of gas chromatographic-mass spectrometric methods using a stable isotope as the internal standard (MacLeod, Green and Seet 1976; Pearce 1976; Lin et al. 1977). We have modified the gas chromatographic-mass spectrometric chemical ionization assay of Lin et al. (1975) for electron impact (Wilson and Domino 1978). Phencyclidine was determined by gas chromatography-mass fragmentography in six dogs and seven monkeys. Aliquots of venous blood were taken over 4 hours in the monkey after 1.1mg/kg and over 24 hours in the dog after 1.0 mg/kg of phencyclidine, i.v. Pentadeuterated phencyclidine was used as the internal standard. In the electron impact mode the most abundant fragments in the mass spectrum of phencyclidine were m/e 91 and 200, and. 96 and 205 in the deuterated phencyclidine spectrum. These fragments were used to quantify the amount of phencyclidine present. In both species, a complex exponential decline of plasma phencyclidine was found in sane animals that fit a two or three compartment open model. In monkeys, the mean biological half life (B phase) was 2.03 hours and in the dog it was 2.1 hours. Compared to the monkey, the dog exhibited considerable emergence delirium. The two species had rather different pharmacokinetics, which may be relevant to the observed differences in degree of anesthesia and recovery.

After our initial analytic successes with phencyclidine, we subsequently developed a highly sensitive and specific method for quantitation of ketamine and two of its metabolites in dog, monkey and human plasma using gas chromatography-mass spectrometry operated in both electron impact and chemical ionization modes. CL-394, the bromo analog of ketamine, was used as the internal standard. We compared these two assays with the gas chromatographic, electron capture assay of Chang and Glazko (1972). Cur results were in complete agreement. However, when dealing with a limited amount of sample, the mass fragmentography assay was superior. We concluded that the use of gas chromatography, electron capture for routine plasma analyses was adequate for ketamine and barely satisfactory for ketamine metabolite I. However, for ketamine metabolite II mass fragmentography was essential for the small amounts in plasma. For urine analyses, gas chromatography, electron capture is quite satisfactory and we recommend it for routine assays (Lau and Domino 1977).

THERAPEUTIC CONSIDERATIONS OF PHENCYCLIDINE OVERDOSE

In our earlier studies in animals (Domino 1964), it was apparent that the behavioral effects of phencyclidine were potentiated by chlorpranazine. Although some of the cardiovascular effects were antagonized by chlorpromazine, others were not. Hence, chlorpromazine was certainly not useful in treating phencyclidine overdosage in man, at least not during the state of acute intoxication. Our subsequent studies in rat and dog (Domino 1978) indicated that diphenhydramine, droperidol, diazepam, tetrahydroaminoacridine (a cholinesterase inhibitor like physostigmine), physostigmine and scopolamine were not very useful antagonists. The status of naloxone as an antagonist is confusing at the moment, for it recently has been shown to antagonize the locomotor stimulant effects of both nitrous oxide and ketamine in mice (Hynes and Berkowitz 1978) as well as to potentiate the hypersensitivity effects of phencyclidine on electroshock in rats (Markowitz and Komestsky 1978).

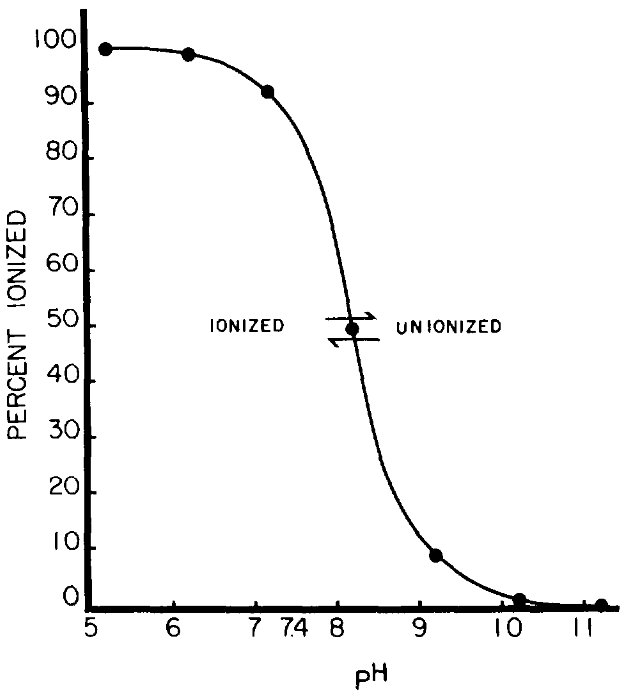
At present we have no specific antidotes to phencyclidine. Obviously much more needs to be done in this area.

Our development of a quantitative gas chromatographic-mass spectrometric assay for both phencyclidine and ketamine led to some very interesting clinical studies. The first relates to phencyclidine. A number of years ago one of my graduate students, Lindsay Hough, and my Research Associate, Ann Wilson, decided to measure the pKa of phencyclidine at room temperature. It turned out to have a pKa of about 8.5. We really need sameone to measure again the pKa of this and related compounds. Verbal communications to me of the pKa of phencyclidine have varied from 8.5 to 9.5.

As shown in figure 6 below, the degree of ionization of this compound varies as a function of its pKa and pH.

Pharmacologists for years have stressed the importance of urinary pH as a functionof the amount of an ionized drug excreted. The ionized form of a chemical does not readily cross the kidney tubules unless there is a specific transport system for it. Hence, basic drugs are ionized in an acid medium and acidic drugs in an alkaline medium. The urinary excretion of basic substances such as nicotine and amphetamines is enhanced in an acid urine and that of acidic drugs such as the barbiturates in an alkaline medium. Although urinary acidification is not the treatment of choice for nicotine or amphetamine poisoning, there is no doubt that this technique is of value, especially in amphetamine overdosage. Hence, this technique should work for phencyclidine. Our task was to prove it with our new phencyclidine assay. Urinary samples fran phencyclidine overdosage cases were obtained from both our own University Hospital in Ann Arbor and from Children's Hospital in Detroit. An account of our experience with the first cases from University Hospital was recently published (Domino and Wilson 1977) and that from Children's Hospital (Done et al. 1977; Aronow and Done 1978; Aronow, Miceli, and Done 1978; Done, Aronow, and Miceli 1978). There is no doubt that acidification of the urine results in enhanced phencyclidine levels, as shown in table 1 for one of our patients from the University Hospital.

FIGURE 6



Percent Ionization of Phencyclidine at Room Temperature as a Function of pH

TABLE 1

EFFECTS OF pH ON HOURLY URINARY EXCRETION OF PHENCYCLIDINE IN A COMATOSE PATIENT

Urinary pH Range		pH	PCP µg/ml	Urine Volume ml/hr	Total PCP Excretion in µg/hr
5.0-5.9		5.3	4.348	300	1304.4
		5.8	.558	520	290.2
		5.6	.812	280	227.4
		5.7	.799	320	255.7
		5.3	.750	350	262.5
		5.4	.767	650	498.6
		5.5	.910	450	409.5
		5.7	.426	450	191.7
	Mean	5.5	1.171	415	430.0
	± SE	±.1	±.457	+45	+129.9
6.0-6.9		6.4	2.089	160	334.2
		6.4	.863	40	34.5
		6.5	.151	1200	181.2
		6.0	.223	700	156.1
		6.5	.167	550	91.8
		6.0	.189	700	132.3
		6.0	.255	450	114.8
		6.0	.302	675	203.8
	Mean	6.2	.503	559	156.1
	± SE	+.1	±.237	±127	± 31.6
	P Value	<.001	NS	NS	<.06
7.0-7.9		7.5	.026	65	1.7
		7.5	.010	60	0.6
		7.2	.032	150	4.8
		7.3	.036	930	33.5
		7.5	.078	570	44.5
		7.9	.036	330	11.9
		7.9	.034	30	1.0
		7.6	.102	670	68.3
	Mean	7.5	.044	351	20.8
	± SE	±.1	±.011	±119	± 8.9
	P Value	<.001	<.03	NS	<.01

Group comparison "t" test of each set of urine values to the most acid urine (pH 5.0-5.9).

The patient was comatose for a period of time and had a great deal of i.v. fluids pushed in order to promote diuresis. In addition, furosemide was periodically given, which accounts for the occasional very large urine volumes obtained for the one hour intervals. All samples were compared to the most acid urine with a pH 5.0 to 5.9. It is abundantly clear that under acidic urine conditions more free phencyclidine is excreted. Inaperiod of 65 hours this patient excreted into the urine 9.46 mg of a total of 500 mg or 1.9 percent of the phencyclidine ingested. This suggests that the majority of this drug may be biotransformed rather than excreted as the free base. Obviously careful quantitative studies must be done in the future.

Aronow and Done believe that urinary acidification is a most effective therapy of phencyclidine overdosage. There are many ways to acidify human urine including ammonium chloride, ascorbic acid, and very dilute i.v. infusion of hydrochloric acid. What seems crucial is that the pH be at least 3 units away from the pKa of phencyclidine to achieve 99.9 percent ionization, which mans a urinary pH of 5.5 or less. This may be difficult to achieve in some patients, which is why we had to resort to i.v. techniques to acidify rapidly. Another very important fact is that the marked skeletal muscle movements that occur during phencyclidine overdosage in man can lead to profound increases in serum creatinine phosphokinase and myoglobin in the urine. Meltzer, Nankin, and Raftery (1971) reported that acute schizophrenic patients showed an increase in serum creatinine phosphokinase. This is the isoenzyme of skeletal muscle. Phencyclidine in a biphasic dose relationship markedly enhanced serum creatinine phosphokinase increases produced by restraint stress in rats (Meltzer 1972). Similar elevations in serum creatinine phosphokinase have been observed by us in documented phencyclidine poisonings that have been accompanied by acute rhabdomyolysis (Cogen et al. 1978). We believe the skeletal muscle injury to be the result of excessive involuntary isometric activity rather than a direct effect of of phencyclidine on skeletal muscle. Our reasoning is that patients who do not have excessive skeletal muscle contractions but still have toxic levels of plasma phencyclidine have much less elevation of their serum creatinine phosphokinase. Skeletal muscle restraints should not be used in patients with phencyclidine overdosage unless the patients are very severe threats to themselves or others. This impression is supported by the study of Goode et al. (1977) that limb restraint markedly elevates serum creatinine phosphokinase and related muscle enzymes in normal volunteers. It is our crude and preliminary impression that acidification of the urine may reduce excessive muscular tonus in phencyclidine overdosage, but this needs to be verified expermentally. What urinary acidification, which is now widely being used, does to the pharmacological actions of phencyclidine and its metabolism is unknown.

Diazepam reduces some of the unwanted cardiovascular and emergence phenomena of ketamine when given as a pretreatment (Zsigmond, Kelsch and Kothary 1976; Kothary and Zsigmond 1976). We have some unpublished observations that diazepam may elevate the plasma levels of ketanine in man. Borondy and Glazko (1977) reported that diazepam interferes with the biotransformation of ketamine in the rat. Our dog studies with diazepam (Domino 1978) indicate that it reduced the convulsions but may have enhanced the central nervous system depression. Hence, unless convulsions are uncontrollable, diazepam would not seem to be indicated in phencyclidine overdosage.

Until a specific antidote for phencyclidine found, those of us dealing with overdose cases will have to be satisfied with symptomatic therapy and urine acidification. However,having helped in the birth and delivery of this drug, I will not rest until that specific antagonist is found.

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Chapter 3

Neurochemical Pharmacology of Phencyclidine

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INTRODUCTION

Phencyclidine (PCP) is an unusual CNS active drug with general anesthetic, psychomotor stimulant, sedative-hypnotic, hallucinatory, and local anesthetic properties. Although PCP is often classed as an hallucinogen, it does not produce the type of visual hallucination associated with the use of LSD or mescaline. Instead, the hallucinogenic activity of PCP is manifested primarily by body image and proprioceptive disturbances often accompanied by thought disorders and changes in affect. The differences between the effects of PCP and LSD are responsible for the classification of PCP as a schizophrenimimetic agent.

Although PCP itself is being abused with increasing frequency, its primary place in the illicit drug market is as an adulterant of other drugs of abuse. In this regard it is the most often encountered drug in analyses of suspect street drug samples. Because of its prevalence, PCP ranks very high on the list of drugs thought to be responsible for drug overdoses. Overdoses of PCP are thought to account for acute psychotic episodes often lasting two or more weeks. PCP overdose often challenges the diagnostic abilities of the clinician, who suffers from lack of a rational pharmacological basis for treatment. Consequently, often the treatment chosen is to leave the patient alone and let the drug effect wear off, which can take days to weeks.

The apparent high abuse liability of PCP and its use as an adulterant of other illicit drugs make it imperative that the scientific community be aware of the effects of acute and chronic administration of PCP as well as the mechanism(s) of action underlying these effects. Most of the known effects PCP administration are apparently mediated through action the CNS. since there is an excellent review of the neurobiological effects of PCP (Domino 1964), the primary purpose of this paper is to review the results of previous studies which have measured the effects of PCP administration on various neurochemical indices of brain function. Deficits in either methodology or experimental design in these studies will also be pointed out. In addition, those areas in which there is no information currently available will be identified.

EFFECTS OF PCP ON BRAIN NEUROTRANSMITTER SYSTEMS

Many, if not all, psychoactive drugs are believed to exert their effects by modifying the transmission of neuronal impulses from one neuron to another. Many neuronal systems have been identified in the CNS which probably use small chemical molecules as mediators of neuronal impulse transmission. Alterations in the concentration, synthesis rate, storage, release, binding, metabolism, and reuptake Of these neurotransmitters after drug administration have been correlated with alterations in the functioning of various neuronal systems. Information regarding the effects of PCP on these neurochemical indices of neuronal function in animals could be important in understanding the mechanism of action of this drug, as well as providing a rationale for treatment of the serious effects often associated with PCP use by humans.

Effects of PCP on Brain Serotonin (5-hydroxytryptamine)

In 1969 Tonge and Leonard compared the effects of PCP, ditran, mescaline, and LSD. At behaviorally effective doses (10 mg/kg, i.p. for PCP) all four hallucinogens elevated serotonin (5-HT) and depressed 5-hydroxyindoleacetic acid (5-HIAA) concentrations in the whole brain of rats. Brain 5-HT concentrations were highest 10 min. after PCP administration and remained elevated throughout the course of the experiment (3 hours). grain 5-HIAA levels were significantly lower than controls 20 and 40 minutes after PCP administration, but were higher than controls 100 and 180 minutes following PCP. It is possible, then that PCP caused a decrease and then a compensatory increase in 5-HT turnover. The method used in this study for assessing turnover prevented the assessment of this possibility. In this study turnover was assessed by following the decline of brain 5-HT after inhibiting its synthesis with p-chlorophenylalanine (PCPA). Control rats were injected with PCPA at time zero and sacrificied either immediately or nine hours later. Experimental animals also received PCP at time zero and were injected with PCP 0, 3, and 6 hours after PCPA and were sacrificed 9 hours after PCPA. The data thus obtained were used to support the hypothesis that PCP reduced theturnoverof 5-HT. Although this may indeed be the case, it is difficult to conclude this fran data collected at two time points. These investigators also observed that PCP had no effect upon two enzymes involved in the synthesis (aromatic amino acid decarboxylase) and metabolism(monoamine oxidase) of 5-HT. I am unaware of any studies which have assessed either the effect of PCP on 5-HT turnover directly (without disturbing the steady-state) or of any which measured the effect of PCP on the first enzyme involved in the biosynthesis of 5-HT, tryptophan hydroxylase. These studies clearly need to be done in order to clarify the effects of PCP on serotonergic systems.

It is now fairly well established that brain 5-HT synthesis is dependent upon tryptophan availability since tryptophan hydroxylase is apparently not saturated with substrate (Eccleston et al. 1965).

In this regard, PCP has been shown to reduce the concentration of both plasma and brain tryptophan about 20 percent (Tonge and Leonard 1970). If 5-HT. synthesis is indeed dependent on brain tryptophan, then 5-HT levels would be decreased rather than increased as these investigators previously indicated (Tonge and Leonard 1969). It is possible, however, that PCP may actually increase the pool of free tryptophan in plasma (i.e., not bound to plasma albumin) available for transport into the brain by competing with tryptophan for albumin binding sites, as other drugs have been shown to do (Gessa and Tagliamonte 1974). This possibility has not been addressed. In another study, Tonge and Leonard (1972) showed that PCP administration to rats at a dose (10 mg/kg) comparable to that used in their 1969 study, produced the opposite effects on 5-HT and 5-HIAA, i.e., 5-HT levels were reduced and 5-HIAA levels were elevated. To further confuse the issue, Tonge (1971) reported that PCP produced the opposite effect on 5-HT and 5-HIAA on populations of Wistar rats obtained from different sources. Using the 5-HIAA/5-HT ratio as an index of serotonergic activity, PCP decreases the turnover of 5-HT in the substrain with the higher 5-HIAA/5HT ratio while increasing the 5-HT turnover in the strain with the lower 5-HIAA/5-HT ratio. Because of the suggestive nature of the foregoing studies with PCP and the proposed role of 5-HT in emotional and psychotic behavior, it is felt that a detailed biochemical study of the effects of PCP on serotonergic function is warranted. It should be noted here that ketamine (a structural analog of PCP) produced either no effect or a slight increase in rat brain 5-HT levels, depending upon the dose administered (Sung et al. 1973). These authors showed a significant decrease in 5-HT turnover, as determined by the method of following the rate of increase in 5-HT after inhibition of its metabolism with pargyline.

Effects of PCP on Brain Catecholamines

Tyrosine, a precursor for both dopamine (DA) and norepinephrine (NE) synthesis, has been proposed to exert some regulatory influence on the synthesis of catecholamines (Wurtman et al. 1974). Tonge and Leonard (1970) have shown that rat brain tyrosine levels were elevated 30 to 40 percent after the administration of PCP. Plasma tyrosine levels, however, were little affected.

In an experimental design which employed the conversion of ^{14}C-tyrosine into ^{14}C-catecholamine, Hitzeman et al. (1973) reported that PCP resulted in significant decreases in the amount of ^{14}C-DA and ^{14}C-NE synthesized, whereas the accumulation of the O-methylated metabolites of DA and NE (^{14}C-3-methoxytryamine and ^{14}C-normethanephrine, respectively) appeared to be increased over control. However, when ^{14}C-DOPA was used as the precursor, no effect of PCP was observed. It was then concluded that PCP probably acts at the level of tyrosine hydroxylase (the enzyme which converts tyrosine to DOPA). Unfortunately, these authors neglected to measure the specific activity of tyrosine. dopamine and norepinephrine. In light of the report by Tonge and Leonard that PCP elevates brain tyrosine, it is entirely possible that these results are the artifactual consequence of a diluted precursor specific activity, rather than an actual decrease in synthesis. The increase in accumulation of the O-methylated metabolites observed suggest that PCP either increases the release or decreases the reuptake of the catecholamines from the extraneuronal space, However, it should be noted that the presumed extreneuronal localization of catechol-O-methyltransferase is presently under dispute.

In a study similar to their study of the effects of PCP on serotonin, Leonard and Tonge (1969) described the effects of PCP on DA and NE. They report that 10 mg/kg PCP produced a substantial decrease in whole brain NE concentration, no charge in normethanephrine, and a slight increase in DA levels. Whereas previously it was demonstrated that PCP protected against reserpine-induced serotonin depletion, in this study PCP was found to potentiate the reserpine-induced depletion of NE. PCP was found to have no effect on the turnover of NE as estimated by inhibiting its synthesis with α-methyl-p-tyrosine (α-MPT) and measuring NE levels at 0 and 3 hours after α-MPT. As was the case with the studies of the effects of PCP on serotonin neurochemistry, the ones on catecholamine neurochemistry suggest that a more rigorous approach would yield less ambiguous data and allow a more meaningful interpretation of the effects of PCP on catecholamine function.

In spite of the studies just discussed which suggest that PCP my have little or no effect on DA or NE function, there are several studies which suggest there may be profound effects of PCP on both of these systems. Taube et al. (1975) reported that PCP inhibited the uptake of ^{3}H-NE by rat cortical slices by 50 percent at 5 x 10^{-6} M. Interestingly, ketamine was about 100 times less potent. This effect of PCP on NE uptake was verified by Garvey and Heath (1976) who used a synaptosomal preparation. These workers demonstrated that PCP is a competitive inhibitor of both ^{3}H-NE uptake by hypothalamic synaptosomes (Ki = 4.7 x 10^{-7}M) and of ^{3}H-DA uptake by striatal synaptosomes (KI = 4 x 10^{-7}M). Very recently these observations were verified and the list of putative neurotransmitters whose synaptosomal uptake is competitively inhibited by PCP was extended to include serotonin (Smith et al. 1977). Ketamine has been shown to be a much weaker competitive inhibitor of synaptosomal uptake of ^{3}H-NE (Smith et al. 1975).

Another interesting study which suggests the involvement of DA in the action of PCP utilized the turning behavior of rats after unilateral electrolytic lesions of the substantia nigra (Finnegan, Kanner, and Meltzer 1976). These authors found that PCP produced a dose-related increase (maximal at 10 mg/kg) in ipsilateral rotation. This effect was attenuated by α-MPT and haloperidol (a DA antagonist), thereby suggesting that this action of PCP is mediated by DA. Unfortunately, in contrast to turning behavior after unilateral 6-hydroxydopamine lesions, this model apparently does not distinguish between presynaptic and postsynaptic drug actions (Costall and Naylor 1971). A cholinergic component of this action of PCP was also identified by the observation that the ipsilateral turning was blocked by the cholinomimetic drug arecoline and was slightly potentiated by the anticholinergic agent trihexyphenidyl. There is considerable evidence that turning behavior (as well as other functions mediated by the striatum) is regulated by a reciprocal relationship between dopaminergic neurons and cholinergic neurons. For example, both direct and indirect dopaminergic agents and anticholinergic agents can induce ipsilateral rotation in this model. Thus PCP may induce rotational behavior by potentiating dopaminergic transmission, by blocking cholinergic transmission, or both.

Effects of PCP on Acetylcholine (ACh)

There has bee-n surprisingly little work done on the effects of PCP on central cholinergic systems, despite the ample evidence obtained in vitro that PCP both antagonizes the ACh receptor and has potent antiacetylcholinesterase activity. One research group from Israel has presented both theoretical and experimental evidence that PCP and ACh have a very similar electrostatic charge distribution pattern when they are considered in the vicinity of the muscarinic receptor (Weinstein et al. 1973; Paster et al. 1974; Maayani et al. 1974). PCP, however, appears to be an antagonist of ACh in the isolated frog rectus abdominis and guinea pig ileum preparations, rather than an agonist. This group has proposed theoretical considerations to account for the antagonistic activity based upon the cyclohexyl ring-induced rigidity of the molecule. Maayani et al. (1974) also demonstrated that PCP competitively inhibits butyrylcholinesterase (Ki = 1 x 10^{-6}M) and acetylcholinesterase (Ki = 80 x 10^{-6}M). The ACh antagonist and anticholinesterase activities would, of course, tend to offset each other. The overall activity of PCP tends to be anticholinergic, however, as evidenced by the observation that PCP-induced anesthesia in the guinea pig and hyperactivity in the muse were both significantly antagonized by tacrine, a potent anticholinesterase (Maayani et al. 1974). Recently this group of investigators reported that scopolamine blocked the development of tolerance in mice to the effects of cyclohexamine, a structural analog of PCP (Pinchasi et al. 1977). In contrast, ketamine was shown to produce a relatively weak reversible mix inhibition of acetylcholinesterase from beef caudate (Ki = 500 x 10^{-6}M) (Cohen et al. 1974). It is unclear whether or not this concentration is physiologically significant since the slight (25 percent) increase in whole brain ACh levels observed by these authors was found to last less than ten minutes. In a study utilizing a cholinergic antisynthesis agent (hemicholinium-3), Domino and Wilson (1972) reported that PCP (10 mg/kg) slightly increases the turnover of ACh but is without effect on the whole brain levels of ACh. Leonard and Tonge (1970) also observed no effect of PCP on whole brain levels. These authors also failed to observe any change in brain cholinesterase activity following the administration of PCP (10 mg/kg).

It is now evident that the synthesis of ACh is dependent upon the high-affinity, sodium-dependent uptake of choline (Yamamura and Snyder 1973; Haga and Noda 1973). An altered choline uptake could conceivably play a role in the cholinergic effect of PCP. To my knowledge no one has studied the effects of PCP on this system.

Effects of PCP on Other Biochemical Parameters

Tonge and Leonard (1970) found that PCP (10 mg/kg) resulted in no change of whole brain levels of histamine or glutamic acid. However, they did detect a decrease in whole brain concentration of γ-aminobutyric acid (GABA) which persisted for two hours after PCP injection.

They observed no effect on GABA after 3 mg/kg of PCP. Interestingly, ketamine has been demonstrated to competitively inhibit glutamate decarboxylase *in vitro*, but to produce no change in either brain glutamate or GABA levels when administered *in vivo* (Dye and Taberner 1975).

There are several other studies documenting effects of PCP on ketamine on a wide variety of biochemical parameters which may be relevant to this review. I will briefly describe two of them. Some studies have previously demonstrated that subgroups of psychotic patients of all diagnostic types exhibit increased serum levels of type III (skeletal muscle) isoenzyme of creatinine phosphokinase (Meltzer et al. 1971). Interestingly, phencyclidine, in a biphasic dose-response fashion, significantly enhanced the increase in serum creatinine phosphokinase levels produced by restraint stress (Meltzer 1972). The magnitude of this effect was rather dramatic in male Sprague-Dawley rats, but not at all evident in guinea pigs. The significance of these studies is uncertain, but at the very least they emphasize that the effects of PCP varies markedly between species.

Anesthetic doses of ketamine have been demonstrated to elicit an increase in rat plasma corticosterone levels similar to that produced by a pharmacological dose of ACTH (Fahringer et al. 1974). This response to ketamine was blocked by hypophysectomy and administration of dexamethasone, and partially blocked by propranolol and haloperidol, but not by atropine or phentolamine. Aside from supporting the notion that this response may be mediated by ß-adrenergic or dopaminergic systems, it brings up the possibility that PCP may also elicit a similar corticosterone response. In light of the observation that tryptophan hydroxylase activity can be increased by corticosterone treatment (Azmitia and McEwen 1969), it is possible that some of the effects of PCP on the serotonergic system may be mediated by this pituitary-adrenal response.

SUMMARY

In view of the diverse pharmacological spectrum of PCP, it is unlikely that the effects of PCP are caused by an alteration in the function of a single neurotramsmitter. Previous studies have suggested that the central biogenic amines, 5-HT, DA and NE, as well as ACh and GABA may be involved either directly or indirectly with the mechanism(s) underlying the behavioral effects of PCP. The information currently available on the neuropharmacological actions of PCP is found to be deficient in many respects. In spite of the several studies which have examined the effects of PCP on neurotransmitter substances in the brain, relatively little is known in an unambigous my. Most of those studies used whole brain for analysis of neurotransmitter concentration. Increases, decreases, or no change in a neurotransmitter concentration for whole brain reveals little or nothing about the functional aspects of the particular neurotransmitter. Interpretation of many of these studies was made extremely difficult by the concomitant use of relatively nonspecific drugs such as tetrabenazine, reserpine, imipramine, etc. Many of these studies failed to correlate their findings temporally with behavioral activity and almost all of these studies neglected to establish a basic dose-response relationship for the observed effect. Furthermore, the effects of chronic administration of PCP, heretofore, have been totally neglected in regard to neurochemical studies. In summary, these studies have only suggested that 5-HT, DA, NE, ACh, and GABA may be involved in sane way in the mediation of the behavioral effects produced by PCP.

As can be seen from the foregoing review of the state of knowledge on the neurochemical pharmacology of PCP is in its infancy. It is felt that future research in this area can provide valuable information about the mechanism(s) of action of PCP only if each neurochemical variable is examined as a function of both dose and time and then correlated with the behavioral effects of the drug. In addition to measuring the effects of PCP on neurotransmitter concentration in discrete brain areas, future studies should not neglect to measure the concentration of neurotransmitter precursors and metabolites. In addition, techniques for determining the turnover of neurotransmitter pools are available Which do not disturb the existing steady-state of the neurotransmitter. It is felt that the proper utilization of such techniques would result in a significant increase in our understanding of the way this important and interesting drug affects the CNS.

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Chapter 4

The Behavioral Effects of Phencyclidine in Animals

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INTRODUCTION

Study of the behavioral pharmacology of phencyclidine (PCP) has accelerated concurrently with the increased public health concerns associated with its illicit use. Some important aspects of the pharmacology of this unusual compound have been revealed by this research, although there remain many more questions than answers. At the conclusion of this paper we will point out some of the future directions which behavioral research with PCP might profitably take. Before doing this, we will describe the current status of knowledge of the behavioral effects of this drug, focusing on research which has appeared since the two previous reviews of this area (Domino 1964; Balster and Chait 1976) and on recent research in our laboratory. Our research has recently been most concerned with two aspects of the behavioral effects of PCP: tolerance development and interactions between PCP and other drugs. Before reporting our results on these two topics, we will briefly summarize some of the important results of prior behavioral work with this drug.

SPECIES DIFFERENCES IN THE BEHAVIORAL EFFECTS OF PCP

One of the most interesting aspects of the behavioral pharmacology of PCP is the obvious species differences in its gross behavioral effects. These differences were noted in the early preclinical studies of PCP by Chen and his coworkers (1959) and are consistently seen in our laboratory. In rats and mice, PCP produces behavioral effects qualitatively similar to those of psychomotor stimulants such as the amphetamines. In rats, for example, intraperitoneal doses above 3 mg/kg produce increased motor activity, while doses between 5 and 10 mg/kg result in repetitive movements, including cage circling, side to side head movements, and repetitive sniffing not unlike the stereotyped behaviors seen with stimulant administration in this species. These behaviors differ from the effects of stimulants, however, in that the animals also are markedly ataxic. A similar constellation of behavioral effects occurs in mice, although mice are, if anything, more stimulated. At intraperitoneal doses above 3 mg/kg they race around the cage, and in the range of 10 mg/kg they run off the edge of any flat surface they are placed on. Convulsions are not uncommon at doses above 20 mg/kg. In our experience, there is no dose of PCP which will produce anything resembling surgical anesthesia in the mouse.

The amphetamine-like properties of PCP in mice have also been seen in schedule-controlled behavior. Wenger and Dews (1976) compared the effects of PCP to the effects of d-amphetamine, pentobarbital and ketamine using a multiple fixed interval fixed ratio (mult. FI-FR) schedule of food reinforcement. The effects of PCP were qualitatively more similar to those of d-amphetamine than pentobarbital in that at some dose both PCP and d-amphetamine increased FI response rate and decreased FR response rate. Interestingly, the effects of ketamine were also very similar to PCP and d-amphetamine. A very similar effect of PCP and ketamine on mult. FI-FR performance has also been reported in the pigeon (Wenger 1976).

Chen et al. (1959) reported that the effects of PCP were different in the guinea pig than in the mouse and rat. Only "calming" effects were seen until cataleptoid or convulsant doses were reached. We, on the other hand, have seen more typical rodent-like effects of PCP in the guinea pig. Intraperitoneal doses in the range of 2 to 4 mg/kg result in increased movement in the normally sedentary guinea pig. At the higher doses repetitive movements can be seen, and ataxia also occurs. One animal exhibited obstinate progression, a continuation of walking movements after reaching the cage wall. In a pilot study, PCP increased motor activity of guinea pigs in a circular runway apparatus (Kenneth M. Johnson, personal communication) .

In rodents, PCP shares other pharmacological properties with psychomotor stimulants. Like methamphetamine and cocaine, PCP increases blood pressure, promotes urination, and decreases electrically induced tonic extensor seizures (Chen, Ensor, and Bohner 1965). In short, PCP looks a great deal like a sympathomimetic which produces ataxia when studied. in rodent species. This similarity of PCP to stimulants led us to suspect that PCP may enhance the behavioral effects of amphetamine in rats. We have found this to be the case (Balster and Chait 1978) and will describe these results in more detail later in this paper.

The gross behavioral effects of PCP in subhuman primates are substantially different from those we described for rodents. In the rhesus monkey, for example, intramuscular doses between 0.2 and 0.4 mg/kg produce mild ataxia and a calming effect. Normally agressive monkeys became easier to handle. Signs of repetitive or stereotyped behaviors are not seen. At doses above 0.8 mg/kg the animals are cataleptic. Nystagmus is frequently seen, and occassionally marked salivation occurs. Although the monkeys are immobile, they may show exaggerated limb and mouth movements, their eyes remain open and most reflexes remain intact. The animals, however, are unresponsive to enviromental events. The sequences of unresponsiveness, gross ataxia, motor restlessness and nystagus is very similar to the effect of large doses in humans.

The gross behavioral effects of PCP in squirrel monkeys are qualitatively similar. Squirrel monkeys, however, are somewhat more sensitive to the effects of PCP on motor coordination. For example, an intramuscular dose of 0.2 mg/kg in the rhesus monkey produces marginal gross behavioral effects. Slight ataxia is seen but the animals are able to grasp objects between their fingers and maintain normal posture with little difficulty. In the squirrel monkey, an even lower dose (0.16 mg/kg/ intramuscularly) producesmarkedincoordination, inability to grasp objects, and inability to sit on their perch without support. In general the effects of PCP in monkeys are quite reliable from animal to animal. We have, however, observed one rhesus monkey who was quite insensitive to the effects of PCP, always requiring doses at least three times higher than normal to produce sedation adequate for handling. We are unable to explain this insensitivity, but it suggests that there are substantial individual differences to the effects of PCP can occur.

In spite of the differences between the effects of PCP on gross behavior of rodents and monkeys, its effects on schedule controlled operant behavior appear qualitatively similar. There has been no systematic research comparing the effects of PCP on operant behavior in various species, but some generalizations can be made based on studies using similar schedules in different laboratories. The most consistent finding so far is that PCP produces a rate dependent effect on fixed interval performance in mice, pigeons and squirrel monkeys (Wenger and Dews 1976; Wenger 1976; Chait and Balster 1978a). Low rates of responding during the early portions of each interval tend to be increased by PCP, whereas higher rates during the later portions of each interval tend to be decreased. During the fixed interval component of complex schedules in mice, pigeons, and squirrel monkeys, overall response rate increases can be seen at low doses. These increases are considerably more dramatic in the mouse than in the pigeon or squirrel monkey, even though average baseline rates in all three species were comparable (0.56 to 0.74 responses/sec.). PCP produces only dose related decreases in fixed ratio response rates in all three species. Although the parameters in these experiments differed somewhat, rough estimates can be made of relative potency of PCP for disruption of fixed ratio performance. These are shown in table 1 along with a comparable value for the rhesus monkey (Balster and Chait 1976).

TABLE 1

DOSES OF PHENCYCLIDINE PRODUCING 50% DECREASES IN FIXED RATIO RESPONDING IN VARIOUS SPECIES OF LABORATORY ANIMAIS

Species	ED 50
Mouse	10.00 mg/kg[a]
Pigeon	0.70 mg/kg[b]
Squirrel Monkey	0.27 mg/kg[c]
Rhesus Monkey	0.08 mg/kg[d]

a. by inspection of dose response curve in Wenger and Dews (1976)
b. by inspection of dose response curve in Wenger (1976)
c. reported in Chait and Balster (19785)
d. by inspection of dose response curve in Balster and Chait (1976)

One interesting point fran this table is the relative sensitivity of the two species of monkey. Even though the squirrel monkey appears slightly more sensitive to the effects of FCP on observable behavior, it is about 3 times less sensitive to its disruptive effects on food-reinforced fixed ratio responding. The significance of this is unclear but it suggests that something different from nonspecific disruption of gross behavior is responsible for the disruption of operant behavior in one or both of these species.

STIMULUS PROPERTIES OF PCP

The stimulus properties of PCP were discussed in our earlier review (Balster and Chait 1976) and there has been very little published on this topic since then. Two studies have demonstrated that PCP can serve as an effective discriminative stimulus in a variety of response choice situations (Jarbe, Johansson, and Henriksson 1975 ; Overton 1975). One of the applications of drug discrimination studies is that they allow drug groups to be classified by virtue of similar discriminative effects using stimulus generalization procedures (Barry 1974; Schuster and Balster 1977). Drug classifications based on discriminative stimulus properties generally follow traditional pharmacological classifications. Stimulus generalization studies with PCP suggest that phencyclidine and related arylcyclohexylamines belong in a class by themselves in that they do not transfer stimulus control to morphine, chlorpromazine, ditran, Δ9-tetrahydrocannabinol and pentobarbital (Jarbe, Johansson, and Henriksson 1975; Overton 1975). Ketamine appears to be qualitatively similar to PCP, and another related compound, N-ethyl-phenylcyclohexylamine (PCE), also transfers stimulus control from PCP. This suggests that PCE may produce effects similar to PCP and ketamine in humans, and we have heard reports of confiscation of street samples of this drug. The classification of arylcyclohexylamines on the basis of their stimulus properties may be a useful way of providing evidence of potential PCP-like abuse in human populations.

Two papers published in 1973 reported that PCP can serve as a reinforcing stimulus in intravenous drug self-administration studies in rhesus monkeys (Balster et al. 1973; Pickens, Thompson, and Muchow 1973). This is particularly interesting in view of the fact that although most drugs of abuse will serve this function, drugs classified as hallucinogens (Deneau, Yanagita, and Seevers 1969; Hoffmeister and Wuttke 1975) and Δ^9-tetrahydrocannabinol (Harris, Waters, and McLendon 1974; Camey, Uwaydah, and Balster 1977) generally do not. This emphasizes the uniqueness of PCP as a "hallucinogen." Recently it has been demonstrated that ketamine is also reliably self-administered by rhesus monkeys (Moreton et al. 1977). This represents another example of the similarity between PCP and ketamine in behavioral studies in animals. A behavioral pharmacological basis for differences in the abuse liability of these two compounds has yet to be found.

PCP INTERACTIONS WITH OTHER DRUGS OF ABUSE

It is important to study the effects of PCP in combination with other drugs of abuse, as multiple drug use is widespread. This may be a particularly important consideration with PCP since street samples of PCP are often mixed with other drugs. The use of PCP concurrent with the use of nicotine, alcohol and marihuana undoubtedly occurs frequently, the former and latter being more common because PCP is often administered by adulteration of smoking materials. PCP combinations with other drugs of abuse are also likely to occur. The possibility of increased toxicity associated with these combinations should be thoroughly investigated.

There have been no behavioral studies of the interaction between PCP and nicotine or alcohol. Such studies are clearly indicated. Pryor et al. (1977) have completed an extensive series of experiments on the interaction between PCP and Δ^9-tetrahydrocannabinol (THC) in rats. In general, PCP enhanced the depressant properties of Δ^9-THC. For example, acute doses of PCP which had little or no effect when given alone, enhanced the effects of Δ^9-THC (1.25 to 2.5 mg/kg intraperitoneally) on conditioned avoidance responding, photocell activity, heart rate and body temperature. On the other hand Δ^9-THC antagonized the motor activity increases produced by a high dose of PCP (5.0 mg/kg).

PCP Interactions with Pentobarbital

We have completed a series of experiments on the interactions between PCP and sodium pentobarbital (PB). We have used a PCP-PB canbination for anesthesia with rhesus monkeys for years. The advantage of this canbination for short surgical procedures is that the dose of PB necessary to reach a surgical plane of anesthesia is reduced 2 to 3 fold. As a consequence the animals recover consciousness in substantially less time than when PB is given alone at higher doses, reducing the risk of postsurgical complications. This use of PCP-PB combinations obviously suggests that PCP enhances the depressant effects of PB; therefore we have sought to examine this interaction in a number of species using a variety of measures.

The results of study (Chait and Balster 1978b) of the effects of PCP on PB lethality in mice are presented in table 2.

TABLE 2

EFFECTS OF PHENCYCLIDINE ON PENTOBARBITAL LETHALITY IN MICE

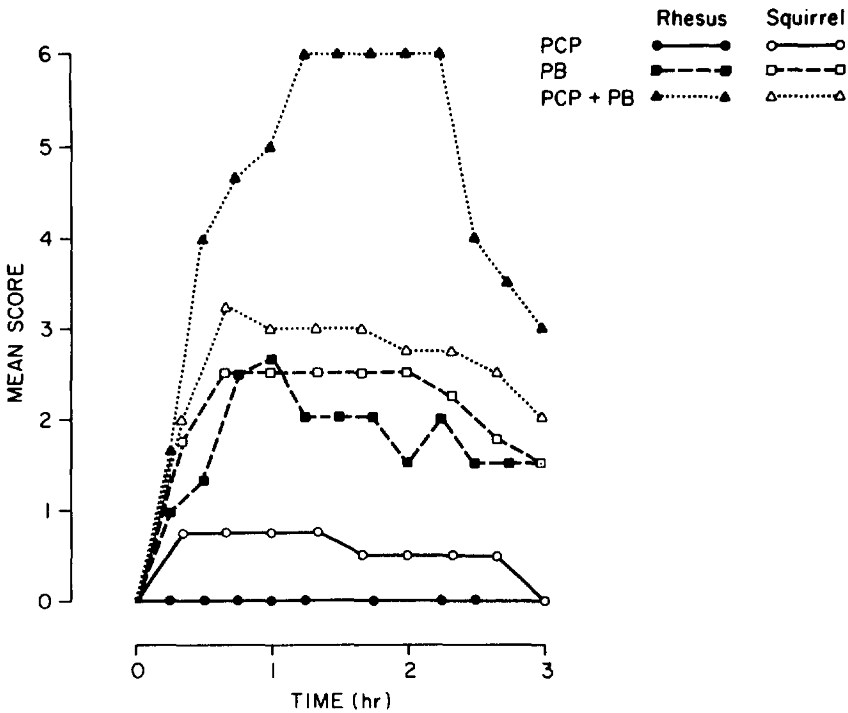
Phencyclidine Pretreatment Dose (mg/kg i.p.)	LD50[a] mg/kg i.p.) of Pentobarbital (±95% C.L.)
0	110 (±23)
3	80 (±16)[b]
30	53 (±12)[c]

a. calculated by the method of Litchfield and Wilcoxon (1949)
b. significantly different from Pentobarbital + Saline ($p<.05$)
c. significantly different from Pentobarbital + Saline and Pentobarbital + 3.0 mg/kg Phencyclidine ($p<.05$)

A dose-dependent enhancement of PB toxicity was observed. The animals appeared to die fran respiratory depression.

We also looked at this interaction in two species of monkeys (Chait and Balster 1978b). A rating scale was designed which reflects degrees of CNS depression produced by pentobarbital. Scale values were: 0- normal movement and posture, l-does not take offered food pellet, 2- unable to climb or maintain a sitting posture without support, 3- unable to sit, 4- unconscious with corneal reflex present, 5- unconscious with no corneal reflex, 6- unconscious with no corneal or pain reflexes (surgical anesthesia). In the squirrel monkey, doses of 0.16 mg/kg PCP and 12.5 mg/kg PB were studied alone and in combination. In the rhesus monkey, doses of 0.2 mg/kg PCP and 25 mg/kg PB were studied alone and in combination. Injections were given simultaneously intramuscularly. The results are summarized in figure 1.

FIGURE 1



Phencyclidine (PCP) -- Pentobarbital (PB) interactions in rhesus and squirrel monkeys

In the rhesus monkey it can be clearly seen that a dose of PCP which has very little effect when given alone markedly potentiates the anesthetic effects of PB. The dose of PB used in this study when given alone only results in some difficulty maintaining a sitting position without support, but combined with PCP produces a surgical level of anesthesia of approximately one hour's duration. The results with squirrel monkeys were quite different. Although the dose of PCP and of PB used both produced greater effects in this species when given alone, there was no evidence of potentiation. This is an interesting and unexpected species difference that warrants further investigation, particularly in light of other data we have collected in the squirrel monkey using schedule controlled behavior in which PCP failed to enhance the response rate decreasing effects of PB (Chait and Balster, unpublished data).

In spite of our failure to find evidence for a PCP enhancement of PB effects in the squirrel monkey, the data from mice and rhesus monkeys raises the question of potential toxicity which may result from combined use of these drugs in human populations, On the basis of the greater phylcgenetic similarity to man of rhesus monkeys, we would, other factors being equal, place more weight on this result. Another question we would raise concerns the specificity of this interaction to PB. Does PCP enhance the depressant effects of other barbituates, nonbarbituate sedatives, benzodiazepines, and alcohol as well? Clearly, further research in this area is indicated.

Phencyclidine Interactions with d-Amphetamine

One benefit of studying drug interactions with PCP is that the results may provide clues concerning the neurochemical mechanism of action of PCP. This is the case with PCP and d-amphetamine interactions. There is some evidence that PCP may possess dopaminergic activity. PCP has been shown to be a potent competitive inhibitor of dopamine uptake in rat striatum (Smith et al. 1975; Garey and Heath 1976). It has also ken shown to produce ipsilateral rotation in rats with unilateral lesions in the substantia nigra, and this effect can be reversed by pretreatment with alpha-methyl-para-tyrosine, haloperidol and pimozide (Kanner et al. 1975; Finnegan et al. 1976). Ipsilateral rotation is generally considered to be indicative of an indirect acting dopamine agonist and is also produced by amphetamines. Since stereotyped behavior produced by amphetamine (and perhaps the amphetamine psychosis as well) is generally considered to be a dopaminergic effect, it might be postulated that PCP would enhance amphetamine sterotypy. We have found this to be the case with low doses of PCP in the rat (Balster and Chait 1978).

In two separate experiments a 9 point rating scale was used to study the effects of various doses of PCP on stereotypy produced by d-amphetamine. PCP at 2.5 mg/kg, which had no effect when given alone, potentiated the stereotypy produced by 1 and 3 mg/kg d-amphetamine. Higher doses of PCP produced ataxia and stereotypies when given alone. These higher doses did not enhance the effects of d-amphetamine. Although these results are preliminary, they are consistent with the hypothesis that PCP has dopaminergic activity and suggest that PCP may enhance the behavioral toxicity associated with stimulant abuse. They may also serve as a starting point in the investigation of commonalities among the model psychoses elicited by amphetamines (Snyder 1972; Ellinwood and Kilbey 1978) and PCP (Luby et al. 1959).

TOLERANCE AND DEPENDENCE WITH PCP

There is conflicting evidence on the degree of tolerance develop ment associated with chronic PCP administration. There is some evidence from the veterinary use of PCP that the duration of anesthesia decreases with repeated use (Martin et al. 1972). We have reported a preliminary study of tolerance development in rhesus monkeys (Balster and Chait 1976). PCP was given daily, seven days a week, over a period of four months at doses beginning at 0.2 mg/kg/day increasing to 1 mg/kg/day. Dose effect curves for PCP effects on food reinforced operant behavior were obtained before and after this chronic regimen. In two of the three monkeys a greater than 4-fold shift in dose effect curve was obtained; in the third monkey, however, there was less evidence for tolerance development. In addition, the duration of observable motor disruption in these three animals after chronic PCP administration was shorter than in untreated monkeys. These same monkeys were observed carefully for signs of withdrawal after discontinuation of PCP. There was no clear evidence of any withdrawal symptomatology.

A more systematic study of the behavioral effects of chronic PCP administration has recently been completed in squirrel monkeys (Chait and Balster 1978a). In this study five squirrel monkeys were given chronic PCP at doses beginning at 0.2 mg/kg once a day increasing to 0.6 mg/kg four times a day (2.4 mg/kg/day) over a period lasting from 82 to 126 days. The regimens of PCP doses more individualized for each subject to maximize tolerance development. Pre- and post- chronic dose effect curves for the effects of PCP on operant behavior revealed approximately a two-fold tolerance development. The most dramatic indication of tolerance was in the duration of PCP-suppressed responding following a dose of 0.6 mg/kg given before and after chronic dosing. At this dose operant behavior was suppressed for an average of 125 minutes before chronic PCP and only 35 minutes after chronic PCP.

As in the study with rhesus monkeys, there was no evidence for disruption of operant behavior after the discontinuation of PCP administration which might indicate a withdrawal syndrome. We had a subjective impression that four of the five subjects demonstrated unusually high excitability and apparent fearfulness (biting, screaming, etc. with handling) during the first or, more commonly, the second day of the withdrawal period, although no systematic attempt was made to quantitate these observations. No changes in body weight or food intake occurred during withdrawal.

On the basis of our studies of chronic PCP administration in two species of monkeys the following conclusions can be drawn. Tolerance can develop to the behavioral effects of PCP: this tolerance is most easily observed as a shortened duration of effect. Tolerance development appears to be in the range of 2 to 4 fold. We have been unsuccessful in pushing the extent of tolerance further. It is important to keep in mind that the chronic regimens we used were designed to maximize tolerance development and would probably represent the upper limits of human abuse pattern. Consequently the degree of tolerance to be expected with less vigorous dosage conditions remains to be seen. At this point we also do not know the mechanism for this tolerance. Pharmacokinetic, pharmacodynamic and behavioral factors may all play a role. Experiments designed to assess the relative contribution of each of these mechanisms are indicated.

A second conclusion to be drawn from our research is the lack of evidence for development of physical dependence. Clear behavioral or autonomic signs of withdrawal comparable to those seen with chronic administration of opioids, barbituates or alcohol have not been observed. Sane suggestion of irritability was observed in the squirrel monkey, however. Systematic studies of potential physical dependence development in various species would be useful in clearly establishing the role dependence may play in chronic PCP abuse.

SUMMARY AND CONCLUSIONS

We have reviewed the current status of our knowledge of the behavioral effects of PCP in subhuman species and have pointed to some areas where more information is most critical. The following tentative conclusions can be drawn: (1) There are marked species differences in the effects of PCP on grossly observable behavior. Various species of rodents show a pattern of response to PCP which is most similar to that of psychomotor stimulants, suggesting that catecholaminergic effects may predominate in these species. The effects in subhuman primates appear to be more "depressant" and qualitatively more like effects in humans, although differences also exist in the response of rhesus monkeys and squirrel monkeys to this drug. In spite of species differences in gross behaviors, the effects of PCP on operant behavior have not been shown to differ qualitatively in different species; however, very little research has been completed that bears upon this. (2) PCP represents a unique class of psychopharmacolcgical agents. The discriminative stimulus properties of PCP do not generalize to drugs fran other pharmacological classes and, unlike other hallucinogens, PCP is self-administered by rhesus monkeys. Studies of the discriminative and reinforcing properties of analogues of PCP in experimental animals may be a useful way of evaluating their dependence liability. (3) PCP has been shown to interact with Δ^9-THC, pentobarbital and d-amphetamine. It enhances the depressant effects of Δ^9-THC, the anesthetic effects of pentobarbital and the behavioral toxicity associated with d-amphetamine administration. (4) With frequent high dose chronic administration 2- to 4-fold tolerance can develop to some of the behavioral effects of PCP, particularly resulting in a shortened duration of action. (5) Preliminary data suggest that PCP does not produce physical dependence comparable to that of opioids or CNS depressants.

ACKNOWLEDGMENT

The research described in this paper was supported by N. I. D. A. Research Grant DA-01442. Larry D. Chait is a predoctoral fellow supported by N. I. D. A. Training Grant DA-07027.

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Chapter 5

Phencyclidine Use Among Youth: History, Epidemiology, and Acute and Chronic Intoxication

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INTRODUCTION

The growing popularity of phencyclidine throughout the United States parallels the early histories of LSD and marihuana. The initial passage of phencyclidine through the drug subculture in 1967 resulted in "bad reviews," attributed to the relative inexperience of drug experimenters. However, during the past three years its popularity has rapidly increased among the now more experienced drug users. In addition, the extensive use of clandestine drug canbinations containing phencyclidine has resulted in part in a marked rise in acute phencyclidine intoxications.

The medical problems emerging from the illicit use of this entirely new class of psychoactive drugs are compounded by its myriad analogs. With the advent of the polydrug abuse phenomenon, the widespread experimental and long-term use of phencyclidine has expanded at an alarming rate. The large quantities of phencyclidine that have been recently confiscated by law enforcement officials in California alone, commensurate with the reported Drug Abuse Warning Network "mentions" and associated deaths, are convincing indicators of a new major drug problem.

This paper will present an overview of the pharmacology of phencyclidine, including its. effects on animals and humans, and the history of its illicit use which is highlighted by factors related to phencyclidine's increasing popularity. Data from three major Federal sources are compared with the results of the authors' hospital-based youth study. The increased problems and deaths seen in a community where phencyclidine has been continuously available are presented and discussed.

A profile of chronic phencyclidine use includes a description of the patterns of use, the phencyclidine experience, tolerance, psychological dependence and side effects, chronic toxicity, and laboratory and neurological findings.

A review of the acute intoxicated state caused by phencyclidine encompasses the presentation, clinical picture and course, laboratory and toxicological findings, diagnosis, management and treatment.

AN OVERVIEW

Phencyclidine hydrochloride (Sernyl), discovered in the mid 1950's (Domino and Luby 1972) is a white, stable solid with a melting point of 234 - 236°C (Domino 1964). It is a weak base that is readily soluble in water (Domino 1964) and highly lipid soluble at physiological pH (James and Schnoll 1976). Animal studies reveal low cellular toxicity and high potency for inducing surgical anesthesia without respiratory or cardiovascular depression in monkeys (Greifenstein et al. 1958).

The drug was first tested on humans in 1957 (Greifenstein et al 1958; Rodin, Luby and Meyer 1958), and when given in doses of 0.25 mg/kg intravenously produced anesthesia sufficient for minor and major surgery (Greifenstein et al. 1958). Phencyclidine was also used as a preanesthetic agent for postoperative analgesia, for pain syndromes, burn dressing, as an abreactive agent, and for the treatment of psychoneurosis. Since the drug produced postanesthetic confusion and delerium of prolonged duration in some cases, clinical investigations were discontinued (Domino and Luby 1972; Chen, Ensor and Bohner 1966).

Phencyclidine hydrochloride in solution was legally manufactured by Parke, Davis and Company for use in humans as a short-acting analgesic and for general anesthesia under the trade name Sernyl (Munch 1974). In 1967 the patent was changed to permit the manufacture by Philips Roxane of the drug in solution as an analgesic for monkeys and other primates under the trade name Sernylan. The Comprehensive Drug Abuse Prevention and Control Act of 1970 classified phencyclidine with the barbiturates and LSD in Section 202(c), Schedule III(b) (7) as . . . "having a depressant effect on the central nervous system" (Munch 1974).

Phencyclidine and its better known derivative ketamine belong to the arylcycloalkylamine group (Chen and Weston 1960) and have a similar spectrum of activity. Administered to animals in increasing doses, these drugs produce excitation, ataxia, catalepsy, general anesthesia and convulsions. The characteristic autonomic actions of these agents, hypertension and tachycardia, appear to be due to central sympathetic stimulation (Chen and Weston 1960).

The degree of central nervous system stimulation and depression and the anesthetic potency vary among the species (Chen and Weston 1960; Chen et al. 1959; and Chen 1965). Based on behavioral criteria, phencyclidine and ketamine act primarily as central nervous system depressants in both humans and monkeys. Immediate excitation does not usually occur, whereas surgical anesthesia is more readily induced in human than in other species (Domino 1964; Chen and Weston 1960; and Chen 1965). Ketamine is less potent, has a shorter duration of action, and produces convulsions less frequently (Chen et al. 1959; Domino, Chodoff and Corssen 1956; and Corssen and Domino 1966).

Phencyclidine is active orally as well as parenterally (IM, IV) in humans (Domino and Luby 1972; and Domino 1964). In several studies involving normal subjects, comparable subanesthetic doses of phencyclidine of 0.1 mg/kg given intravenously over 2 - 12 minutes or 7.5 mg orally consistently produced decreased touch, pain and position sense associated with nystagmus, ataxia and hyperreflexia (Domino 1964; Luby et al. 1959; and Davies and Beech 1960).

Impairment or increased threshold of audiometry, perimetry, visual acuity and taste is seen (Danino 1974). Touch sense and two-point discrimination were found to be the earliest, most pronounced and persistent sensory effect in one study. Changes in muscle tone ranging from a slight increase to catatonia and rhythmic motor behavior have been reported (Luby et al. 1959). An increase in the diastolic blood pressure of less than 10 mm with an increase in pulse rate of generally 20 - 30 beats per minute were also noted. Side effects included nausea with repeated vomiting, vertigo, ptosis and diplopia.

With intravenous administration over five minutes, effects are immediate, with prominent symptoms; lasting 1 - 2 hours (Luby et al. 1959). Following oral administration, subjects have reported changes in their physical or psychological state within 45 minutes with maximum effects at 90 minutes (Beech, Davies and Morgenstern 1961). In a similar study of five obsessional patients,given 5 to 10 mg phencyclidine orally, the point of onset at 30 - 60 minutes and a duration of 1 - 3 hours were reported (Davies 1961).

Given intravenously in anesthetic doses of 0.25 mg/kg (or a total dose of 17.5 mg) over thirty-five minutes, phencyclidine increases the minute volume, rate and depth of respirations of law order. A mean increase in minute volume of 1140 cc was measured in seven normal patients. Their tidal volume and respiratory rates increased a mean of 15.3 and 2.57 cc, respectively. A consistent and significant mean increase of 26 mm Hg in systolic and 19 mm Hg in diastolic pressure was observed. The pulse rate change was significantly increased in three subjects and decreased in three subjects (Greifenstein et al. 1958).

In surgical patients given 20 mg of phencyclidine intravenously following premedication with pethidine and atropine, no response to pain appeared after a few minutes, and most patients were completely unresponsive for periods up to ninety minutes without respiratory depression (Greifenstein et al. 1958). Intravenous doses of 0.275 mg/kg to 0.44 q/kg produced anesthesia for an average of 25 minutes in 735 patients. The duration of surgical anesthesia with 0.5 - 0.75 mg/kg of ketamine is less than 5 minutes with recovery in 1/2 to 1 hour (Chen, Ensor and Bohner 1966).

As a local anesthetic, phencyclidine is approximately equal to procaine. However, the analgesic activity of the arylcyclohexylamines cannot be assessed in animals by standard testing procedures. It has been suggested that their mechanism of action may differ from the narcotic or the analgesic and anesthetic doses are too close to differentiate (Chen, Ensor and Bohner 1966).

In subanesthetic doses there is general impairment of sensory function with a decrease in the appreciation for touch and pain the earliest and most pronounced effects. Subjects are awake and able to communicate with movement preserved and impaired only by ataxia and occasional catatonia until consciousness is lost when higher anesthetic doses are administered. Dissociation between sensory and motor functioning at subanesthetic doses, implying a disturbance of sensory-motor coordination, appears to occur.

Electrophysiologically, phencyclidine and ketamine induce a continuum of subcortical and cortical (EEG) changes in animals, with catatonia or immobility, consistent with central nervous system stimulation. In animals and epileptic human subjects with implanted depth electrodes, limbic arid temporal electrical seizure activity has been observed following ketamine administration. The electrical seizure activity is not always substantiated by convulsive behavior or reflected in the conventional surface EEG (Ferrer et al. 1973; and Winters et al. 1972).

The arylcyclohexylmines also have anticonvulsant properties, antagonizing electrically induced tonic extensor seizures in mice in doses causing ataxia and excitation, and suppressing pentylenetetrazol-induced, initial clonic seizures only at doses approaching anesthetic levels. These properties are related to effectiveness against generalized motor seizures in humans (Chen 1973).

Electroencephalographically, phencyclidine causes diffuse theta and delta slowing in humans. In subanesthetic to anesthetic doses paroxysmal activity is not evident. Changes induced by intravenous infusion ranged from slight theta slowing in one of four volunteers at 0.03 mg/kg to marked theta activity with a dominant medium voltage of 4 - 5 Hz rhythm in two volunteers given 0.2 mg/kg. The onset of frequency changes and their restitution in the electroencephalogram were either gradual and stepwise or abrupt. These effects ranged in duration from 15 to 60 minutes depending on the dose administered and the magnitude of the changes induced.

In six persons given intravenous infusions of phencyclidine, a decrease in fast activity occurred after 2 - 3 mg. At approximately 7 - 10 mg, a diffuse predominant slowing in the occipital, temporal andparietal regions was observed. In the initial clinical trials, doses of 1.0 mg/kg intravenously produced clinically observed seizure activity (Greifenstein et al. 1958).

In humans, phencyclidine has psychotomimetic properties. The toxic psychosis induced by low doses is characterized more by the overt symptoms of schizophrenia than by hallucinations. Reproducing more of the primary symptoms than other drug models, the psychosis produced in normal volunteers is difficult to distinguish from schizophrenia (Domino and Luby 1972; Collins, Gorospe and Rovenstine 1960; and Luisada and Reddick 1975). Extreme exacerbation of existing psychoses followed the administration of phencyclidine to chronic schizophrenic patients (Collins, Gorospe and Rovenstine 1960; and Luisada and Reddick 1975). The drug intensified disorder in thought processes and stimulated considerable affect. Patients acted out sexually and became more active, assertive and hostile. These behavioral changes continued for one month (Luby et al. 1959).

Phencyclidine produces unique and profound alterations of thought, perception and mood in subanesthetic doses. The mental effects in normal volunteers include changes in body image, loss of ego boundary, and depersonalization associated with feelings of estrangement, isolation and dependency (Luby et al. 1959; and Davies and Beech 1960).

Affectively charged experiences are often evoked and some subjects exhibit negativism and hostility or apathy (Luby et al 1959; and Davies and Beech 1960). Thinking is slowed with disruption of attention span, inability to sustain organized directed thought (Davies and Beech 1960), and impairment of learning. Subjects are distractible and perseverate. Time appreciation is disturbed, with underestimation of time intervals. Echolalia, neologisms, and word salad may be observed with a loss of time "boundness." Some subjects manifest echopraxia and repetitive motor behavior (Luby et al. 1959).

Reaction time, tapping speed, rotatory pursuit performance and weight discrimination have been reported to be impaired (Davies 1961).

The oral "sedative" dose for humans is considered to be between 1 - 5 mg. Following oral administration of a subanesthetic dose of 7.5 mg, subjects report changes in their psychological or physical state within 45 minutes and maximum effects at 90 minutes (Beech, Davies and Morgenstern 1961).

Under conditions of sensory isolation or reduced visual, auditory and tactile stimulation, less disturbances of behavior and psychological processes are evident. Subjects experienced only minimal body image changes and felt more in control and less anxious. They were less productive verbally and appeared quieter and calmer. They reported experiencing "nothingness" or "emptiness." When the sensory isolation was stopped, subjects were immediately aware of the perceptual distortions and became more disturbed. Some subjects then experienced nausea or exhibited catatonia.

Following anesthetic doses of phencyclidine, patients were amnesic for both surgery and the recovery period.

The psychotomimetic effects of phencyclidine are most apparent following administration of low doses. The anesthetic properties of the drug associated with changes in the level of consciousness predominate after high doses.

Profouud behavioral effects are seen in several species following phencyclidine administration (Balster and Chait 1976). In the monkey, reinforcing properties have been demonstrated by the initiation and maintenance of lever-pressing for injections of phencyclidine. The drug is self-administered in amounts producing a state resembling general anesthesia (Balster and Chait 1976; and Balster 1976). It is the only "hallucinogen" reliably self-administered by monkeys, which suggests a potential for abuse (Domino and Luby 1972; Luby et al. 1959; and Balster and Chait 1976).

Learned behavior in animals is sensitive to impairment or disruption by phencyclidine (Danino and Luby 1972; Rodin, Luby and Meyer 1958; Chen, Ensor and Bohner 1966; Munch 1974; and Balster and Chait 1976). Discrimination studies indicate that the arylcyclohexylamines produce effects in animals different from other psychoactive substances and probably constitute a distinct class of drugs (Chen and Weston 1960; Chen et al. 1959; Domino, Chodoff and Corssen 1965; Balster and Chait 1976; and Corssen and Domino 1966).

Repeated administration of phencyclidine to monkeys and primates has resulted in shortened periods of effective anesthesia after several weeks or months of use. A similar tolerance to the anesthetic effect of ketamine has been reported (Luisada and Reddick 1975). In monkeys receiving ketamnie 3 - 5 times per week for 6 months, the duration of anesthesia was decreased by 40 percent. Juvenile chimps receiving 3 doses in a one-week period required 50 percent more ketamine to maintain the anesthetic effects (Luisada and Reddick 1975). Similar observations have been made in humans with repeated use of ketamine anesthesia in the treatment of burns (Chen and Weston 1960).

There is some recent evidence of tolerance development to the duration and intensity of the effects of phencyclidine on operant behavior in monkeys with daily administration over a 4-month period. Studies examining physical dependence to phencyclidine associated with the chronic intoxicated states do not appear in the literature (Balster and Chait 1976).

In various animal species, phencyclidine has a relatively short duration of action (Domino 1964). In the monkey, for example, it is rapidly metabolized and excreted in the urine as conjugated di- and mono-hydroxy metabolites (Ober et al. 1963; and Glazko 1967).

After single intravenous doses, 60 percent of the radioisotope labels were recovered in the urine within twelve hours, and approximately 75 percent in eight days (Ober et al. 1963). In humans, the relative concentrations of mono-hydroxy metabolite and the parent compound phencyclidine recovered in urine after acid hydrolysis and assayed by gas liquid chromatography were 68 percent and 32 percent, respectively. No di-hydroxy metabolite was evident (Ober et al. 1963). Subsequently, two mono-hydroxyl metabolites were detected in urine from patients acutely intoxicated with phencyclidine after enzymatic hydrolysis (Lin et al. 1975). There is no evidence that these two compounds possess cataleptic anesthetic activity.

Tissue distribution studies in animals demonstrate relatively high and persistent concentrations in adipose and brain tissue with lower and rapidly falling blood concentrations (Lin et al. 1975; and Corssen and Domino 1966). These results are consistent with the drug's pKa of 8.5 and lipid partition coefficient at physiological pH (Done et al. 1977). The half life in rat blood after IP injection is approximately 3 1/2 hours. The drug concentration half life in the dog followed intravenous administration is approximately one hour (Lin et al. 1975).

No evidence of acute cellular toxicity was reported in the first 1,000 patients who received phencyclidine as an investigational drug. However, phencyclidine with restraint stress produced increased muscle enzyme (CPK, aldolase) levels and skeletal muscle pathology in rats. One of seven human subjects had an increased CPK level following phencyclidine administration.

In acute phencyclidine intoxication with coma, CPK levels greater than 500 units are frequently found. In several cases where CPK has been above 20,000 units, rhambdomyolis preceded myoglobinuria and renal failure. Whether this represents direct muscle toxicity or is secondary to coma and muscle compression is unknown.

Evidence of hematologic, hepatic or renal toxicity was not found by the authors in their study of chronic use of phencyclidine for periods greater than 6 months andupto 5 1/2 years by history.

Several female patients seen by the authors have by history used phencyclidine regularly preceeding and during pregnancy with their infants being in apparent good health. One infant born to mother who used phencyclidine regularly just prior to delivery exhibited poor feeding, a poor sucking reflex and irritability.

Phencyclidine can be detected in concentrations of 1:1000 after extraction with an organic solvent fran an aqueous solution by a color reaction with gold branide or potassium permanganate (Munch 1974). The drug has been identified and quantitatively determined in extracts of body fluid (blood, urine, CSF) and. tissues by thin layer chromatography, gas liquid chromatography with flame ionization detection, and with gas chromatography - chemical ionization mass spectrometry (James and Schnoll 1976; Reynolds 1976; and McLeod, Green and Seet 1976).

The History of Illicit Phencyclidine Use

Street preparations of phencyclidine have continuously changed in name, physical form, and content.

Phencyclidine is sold on the West Coast by such labels as Angel Dust, Cannabinol, Crystal, PCP and THC (Lundberg, Gupta and Montgomery

1976; Radcliff 1975; Perry 1975; Burns et al. 1975; and Burns and Lerner 1976). In the Midwest, among its street names are DUST, TAC and TIC (Drug Enforcement Administration 1975). On the East Coast phencyclidine is sold as Angel Dust, Erth, Green, KW and Sheets. Recently phencyclidine has been identified as being present in samples sold under 46 different names (See Table 1). Many of these street nomenclatures are regional while others arenationalin scope. Although phencyclidine is represented under a multitude of names, the most consistent misrepresentation is "THC" (Burns et al. 1975; Burns and Lerner 1976a, Burns and Lerner 1976b, and Lerner and Burns 1978).

When sold as THC in tablet or powder form the color may be beige, brown, blue, green, orange, pink, red, strawberry, white or yellow. Phencyclidine sold as PCP usually appears beige, gray brown, orange, speckled pink, tan white, white gray or white yellow in color. Physical form varies fran the frequent tablet, powder, crystalline, and granular amorphous solid to the rare liquid.

Phencyclidine has appeared on the illicit market as a powder, a tablet, a leaf mixture (Lundberg, Gupta and Montgomery 1976; and Radcliff 1975), a liquid, and one gram "rock" crystals. The crystalline or granular form is found most frequently in capsules. Phencyclidine on parsley, mint, oregano or other leaves is usually found in the form of a joint. Most street preparations contain the hydrochloride salt, although phencyclidine as the free base has been seen (Shulgin and MacLean 1976).

Since 1975, only 25 percent of the street drug samples containing phencyclidine have contained additional drugs, a smaller percentage than in earlier years. In 1971 - 1974, other drugs were found in 40 - 60 percent of street samples analyzed at the Street Drug Information Program at the University of Southern California of Medicine. LSD was present in 86 percent of all combination preparations, with the "caine" drugs accounting for another 4 percent. Four percent of the samples contained two or more additional drugs. Phencyclidine was mixed with marihuana in only two of 317 samples (Lundberg, Gupta and Montgomery 1976). This trend has also been reflected in other street drug analysis programs across the United States. Recently, phencyclidine and its thienyl analog (TCP) have been identified in over 10 percent of all samples analyzed at the University of Southern California. Only 3 percent of the samples containing phencyclidine were actually sold under the designation.

The crystalline or granular powder form is found most frequently as Crystal or Angel Dust, which usually contain 50 - 100 percent phencyclidine. Found under other names, the purity drops to a range of 10 - 30 percent. Most tablets contain approximately 5 mg and tend to range from 1- 6 mg (Lundberg, Gupta and Montgomery 1976; Radcliff 1975; and Drug Enforcement Administration 1975). Leaf mixtures have been found to contain between 0.24 - 7.9 percent phencyclidine, averaging 1 mg phencyclidine per 150 mg leaves (Lundberg,

TABLE 1

NAMES GIVEN FOR MATERIAL CONTAINING PCP-TCP

Name
Amphetamine
Angel Dust
Belladonna
Cocaine
Cadillac
Cannabinol
Crystal
Cyclones
Detroit Pink
DMT (N,n-dimethyltryptamine)
Dust
Elephant tranquilizer
Erth
Gocn
Green
Hashish
Hog
Horse tranquilizer
Killerweed
KJ crystal
KW
LSD (lysergic acid diethylamide)
Marihuana
MDA (3,4-methylenedlaxyamphetamine)
Mescaline
Mintweed
Mist
Monkey Dust
PeaCe Pill
PCPA (para-chlorophenylalamine)
Peaceweed
Peyote
Psilocybin
Rocket fuel
Scuffle
Sheets
Snorts
Soma
STP (3-methyl-2,6-dimethoxyamphetamine)
Superweed
Surfer
T
TAC
THC (tetrahydrocannabinol)
TIC
TT-1

Gupta and Montganery 1976).

Phencyclidine is taken orally, by inhalation (smoking), insufflation (snorting), and rarely by the intravenous route.

Street samples analyzed have contained phencyclidine in combination with other drugs (barbiturates, ethyl alcohol, heroin, cocaine, amphetamine, methaqualone, LSD, mescaline, procaine). Combination preparations which contained phencyclidine (phencyclidine-procaine, phencyclidine-marihuana, phencyclidine-caffeine, phencyclidine-cocaine, phencyclidine-doxepin, phencyclidine-LSD, phencyclidine-LSD-mescaline, phencyclidine-LSD-aspirin, phencyclidine-LSD-procaine and some 4-5 drug combinations) have also appeared on the illicit market. In addition the presence of PCC (1-piperidinocyclohexane-carbonitrile) as a contaminant in some illicit phencyclidine preparations has been detected (Helisten and Shulgin 1976).

The information needed for the preparation of phencyclidine was reported over 50 years ago with descriptions of the reaction of 1-piperidinocyclohexanecarbonitrile (PCC) with Grignard reagents (Shulgin and MacLean 1976). The majority of the illicitly synthesized phencyclidine is prepared according to the general directions of Kalir and modified in details as required by the availability of chemicals and equipment. Until recently most batch operations were limited by the amount of piperidine to be used (usually a maximum of 500gms) and would produce on a 3 - 5 mole scale (Shulgin and MacLean 1976).

Piperidine was felt to be the most guarded reagent and the easiest to trace and for these reasons manufacturers would pay as much as $1,000/kg for a non-traceable bottle. Now piperidine is no longer the "limiting step" as it has become readily available, leading to the manufacture of larger quantities of phencyclidine.

In addition, a new solvent for distillation that should prevent fires and explosions is now available. Manufacturing is now done in larger, better equipped laboratories that are capable of producing great quantities of phencyclidine. Illegal laboratories containing as much as 25 million dollars worth of phencyclidine have been raided. The last major seizure (in the Los Angeles area) of an illicit laboratory in 1977 yielded 900 pounds of phencyclidine.

Recently an illegal laboratory was raided by the Drug Enforcement Administration in the Michigan area. Officials estimated that the $200 investment in chemicals could produce phencyclidine worth approximately $200,000 on the street.

According to the Drug Enforcement Administration, major production centers have been discovered in Washington, D.C., Detroit, Los Angeles and San Francisco.

Complex and formal distribution systems now exist which mirror the heroin connection. In some areas phencyclidine has surpassed heroin in street price. The same criminal elements that are selling opiates are now also selling phencyclidine. Phencyclidine sold as THC or Angel Dust is usually worth from $25 - $200 per gram and upwards of $1000 an ounce. Individual phencyclidine joints vary from $1 - $20 or more.

Various patterns of phencyclidine use have emerged over the past several years. First time users report stoking a cigarette containing phencyclidine unknowingly or in an experimental fashion. Although the occasional or recreational use pattern is seen, its development is mediated by an initial experience of unexpected and unpleasant effects (Burns et al. 1975; and Burns and Lerner 1978). In areas where the drug has been continuously available, it has gained a preferred drug status with small cluster groups of individuals who have used it on a chronic, daily basis for periods of six months to six years (Burns et al. 1975; and Bums and Lerner 1978). Requests for the authors services through a national consultation service (Lerner, Bums, Linder and Associates) reveal chronic users in California, District of Columbia, Hawaii, Kansas, Kentucky, Maryland, Nevada, and Washington.

In the San Francisco - Oakland area chronic users purchase phencyclidine in gram amounts ranging from $85 - $125 per gram. Money for the purchase of phencyclidine is generally provided by a partner through dealing, hustling, or Social Security Insurance (SSI). Wholesale dealer's costs average fran $40 - $50 per gram, $200 - $300 per quarter ounce, and from $700 - $1,000 per ounce.

Factors Related to Increased Phencyclidine Popularity and Use

When phencyclidine made its illicit debut in 1965 it was marketed as a mild psychedelic. Dealers described this new drug as a mild psychedelic, "a little stronger than marihuana," and sold it in tablet and capsule form. The effects were often unexpected. Since the dosage could not be titrated, users often experienced an adverse reaction. Hence, phencyclidine gained a bad reputation and subsequently was not seen on the streets.

By 1972, a change was observed in both themethodof use and the attitude of users about the drug. A conversion had taken place from using phencyclidine orally in tablet or capsules to smoking it on leaf material. By this newly discovered method the user was able to more effectively control the dosage, thus decreasing the chance of overdose. Experienced users for the first time were able to inform new users how to take it effectively and to describe what the effects would be like. As first time users were now being prepared for this unique experience and with better methods of controlling the dosage, the popularity of phencyclidine spread rapidly. Illicit laboratories increased in proportion to the new demand for material.

Because of the ease of manufacturing phencyclidine in clandestine laboratories, its availability has dramatically increased. Youth are now using phencyclidine in social settings in a similar fashion to marihuana. As other drugs of abuse become difficult to obtain, phencyclidine in many areas is continuously available. Hence, groups of users are likely to select phencyclidine as their drug of choice and to share it with their friends.

Due in part to the lack of full infomation about the effects and dangers associated with phencyclidine,the drug continues to expand in popularity among youth. In general, users are still under the misconception that phencyclidine is merely "a little stronger than marihuana." Young users who were questioned about the differences between LSD and phencyclidine uniformly responded that LSD was a much more dangerous drug and that they would not use it. Phencyclidine, however, does not have this connotation. until this is changed, usage is likely to continue to increase.

The abuse of phencyclidine and other arylcyclohexylamines has emerged over the past 12 years. As stated earlier, phencyclidine was first seen illicitly in 1965, in Los Angeles (MacLean 1977). Two Years later it appeared in San Francisco under the guise of the "PeaCe Pill" (Bums et al. 1975). With media coverage of the adverse effects, phencyclidine disappeared from the street scene in the San Francisco area in 1968, at which time it surfaced on the East Coast under the guise of "Hog." Since then it has been seen with increasing frequency throughout the United States.

In 1969, the N-ethyl analog of phencyclidine, PCE, cyclohexamine appeared on the streets in Los Angeles (Shulgin and MacLean 1976).

By 1972, due to the "ripple effect," phencyclidine appeared in five states, from California to New York (see Table 2). It should be noted that the PharmChem Research Foundation, which provided this data, is only one of many street drug analysis programs operating in the United States. Therefore, the epidemiology of its abuse is riot necessarily reflected by these figures. Louisville, Kentucky, and Eugene, Oregon presented the greatest increases in street drug samples containing phencyclidine.

In 1974, the Thiophene analog of phencyclidine, TCP, was first identified in Hawaii. That same year phencyclidine had spread into another four states.

By 1975 the use of both phencyclidine and TCP had spread to 22 states. TCP was sold on the West Coast in Los Angeles, Newport Beach, Santa Cruz and Sacramento. Outside of California, TCP was being sold in Eugene and Coos Bay, Oregon, and Seattle and Tacoma, Washington.

In 1976 phencyclidine appaared in another two states. The use of TCP decreased slightly, although it remained popular in Oregon and Washington

During the first eleven months of 1977, phencyclidine was identified in 28 states, exceeding all prior years. For the first time samples of phencyclidine were received from Indiana, Kansas, and Nevada. Since these samples were in the powder form, the possibility of

TABLE 2

DISTRIBUTION OF PCP-TCP BY STATE*

STATE	1972	1973	1974	1975	1976	1977**
Alabama				X	X	
Alaska			X		X	
Arizona		X		X	X	X
Arkansas						
California	X	X	X	X	X	X
Colorado	X	X	X	X	X	X
Connecticut					X	X
Delaware						
District of Columbia					X	X
Florida	X	X	X	X	X	X
Georgia		X	X	X	X	X
Hawaii			X	X		
Idaho						
Illinois		X	X	X		X
Indiana			X	X	X	X
Iowa			X		X	X
Kansas						X
Kentucky		X	X	X	X	X
Louisiana						X
Maine	X					
Maryland					X	X
Massachusetts		X			X	X
Michigan		X	X	X	X	X
Minnesota			X			
Mississippi						
Missouri						
Montana		X		X		
Nebraska						
Nevada						X
New Hampshire				X		X
New Jersey				X	X	X
New Mexico						
New York	X	X	X	X	X	X
North Carolina		X				
North Dakota						
Ohio		X	X	X	X	X
Oklahoma			X	X	X	X
Oregon		X	X	X	X	X
Pennsylvania			X	X	X	X
South Carolina						
South Dakota						
Tennessee			X			X
Texas		X	X	X	X	X
Utah					X	
Vermont						
Virginia			X	X		
Washington		X	X	X	X	X
West Virginia						
Wisconsin		X				
Wyoming						
TOTAL STATES	5	17	21	22	24	28

* As confirmed by street drug analysis
** Reporting period January - November

sophisticated chronic use was evident. Although they were Pharm-Chem's first samples from these states, it is unlikely that phencyclidine had not been available previously. For example, although PharmChem's first sample from the Kansas area was received in 1977, the number of cases seen by the District Attorney's Office in Plathe, Kansas, had doubled during that year.

Recently PHP 1-(1-phenylcyclohexyl)pyrrolidine was identified on autopsy in the body of an individual who was shot and killed by a police officer in Los Angeles - the first documented street appearance of this analog.

Demography - Epidemiology of Illicit Use

A dearth of literature exists on the nature and extent of use of phencyclidine and its 30+ analogs. The major Federal sources for determining changes in emerging drug trends are the Client Oriented Data Acquisition Process (CODAP), the Drug Abuse Warning Network (DAWN), and the National Youth Polydrug Study (NYPS).

The CODAP system provides the largest available national data base of patients in treatment. All drug abuse treatment and rehabilitation programs receiving Federal funds are required to collect and report data.

Drugs of abuse are divided into 14 categories. Phencyclidine is classified incorrectly as a hallucinogen, with LSD, mescaline, MDA, DMT, musuhrooms, peyote, and other drugs. Since CODAP has no flexibility in identifying and analyzing phencyclidine independently from the other drugs, this data source is not useful for our purposes.

The DAWN system has been in operation since the spring of 1973. Hospital emergency rooms and inpatient units, crisis centers and medical examiners (coroners) in 24 selected Standard Metropolitan Statistical Areas (SMSA's) are contracted to report incidents of adverse drug reactions to the DAWN central office. In each report, the victim's age, sex, race, employment and treatment status are noted, as well as the drug used, the route of administration, the source of the drug, and the form in which it was acquired.

DAWN data, however, includes only those phencyclidine users who hadadversereactions that required agency intervention. There is no record of the user who ingests phencyclidine without an adverse reactionor who handled such a reaction without agency intervention.

Also, the DAWN data are collected only in the major SMSA's. As an example, in California, DAWN data are collected only for the Los Angeles, San Francisco - Oakland and San Diego areas. Data are not available fran 51 of California's 58 counties. Even within these reporting counties the DAWN reporting system- emergency rooms, inpatient units and crisis centers - is not complete. That is, within these communities many phencyclidine-related problems are treated that are never reported to DAWN.

Those phencyclidine cases which are reported frequently lack complete information. The victims are often not in sufficiently stable condition to respond properly to questions and are not commonly reinterviewed upon recovery.

Fran September 1972 through March 1973, phencyclidine was ranked as the twenty-third most abused drug in the DAWN system. During the period fran April 1973 through March 1974, it rose to the twenty-first position. By the following year, April 1974 through April 1975, phenyclidine use had increased to the fifth position. For the reporting period from May 1975 through April 1976, phencyclidine continued to rank overall as the sixteenth most frequently abused drug. For the youth population between 12 and 18 years of age, however, it was in tenth place.

For this youth population between February and May 1976, there were 294 patients treated in emergency rooms, 330 patients seen in crisis centers, and 2 patients seem by coroners. During the same period phencyclidine ranked as the eleventh most frequently abused drug in Philadelphia and Washington, D.C.; seventh in Chicago and Cleveland; fifth in Minneapolis and Los Angeles; fourth in Detroit; and first in the San Francisco - Oakland area.

White males (61 percent) are twice as likely as white females (32 percent) to report to DAWN emergency room. For crisis centers, however, white males and females are reported at approximately the same rate, 42 percent. The use of phencyclidine by minorities accounts for only 6 percent of the mentions from crisis centers and 7 percent from emergency rooms.

Ninety-one percent of phencyclidine users seen in crisis centers reported their source as a "street buy," whereas with emergency rooms only 49 percent reported "street buys" as their source.

The prime motivation for phencyclidine use among patients seen in both crisis centers and emergency rooms is for the "psychic effects," which account for 73 percent of the mentions. Phencyclidine users from the crisis centers are much more prone (28 percent) to report dependence as their motivation than are the users from emergency rooms (2 percent).

Crisis centers data indicate that the age group of 12 to 13 years for white females seems to be at particularly high risk. Furthermore, 42 percent of the phencyclidine mentions in this age group reported dependence as their prim motivation for use.

Fran September 1976 to March 1977, youth from 12 to 18 years of age were interviewed on admission for drug treatment as part of the NYPS. In all, 2750 patients from 97 treatment program in 39 States participated in this study.

These patients represented a national sample of youth in treatment from all regions, and from the major treatment modalities. They were sampled selectively for sex, race, and ethnic grouping by geographic region. Information contained in this new data base is the most comprehensive data available on youthful abusers.

There is a high degree of similarity between the NYPS sample and the CODAP youth subsample. Hence, information obtained from the NYPS on drugs of abuse such as phencyclidine that are not reported separately in CODAP may now best estimated using this new data source.

PCP Use Within the NYPS Sample

Of the 2750 clients under 19 years of age in the NYPS sample, 857 (31.8 percent) reported having ever used PCP, with 561 reporting the use of PCP during the three months prior to admission. The prevalence of PCP in this sample is the highest reported in any national sample for adults or for youth. PCP ranked seventh in prevalence among the fourteen types of drugs in the sample, and it was abused more frequently than many other well known substances such as inhalants (abused by 28.9 percent of the sample), other sedatives (abused by 28.8 percent), or cocaine (abused by 25.8 percent). A comparison of PCP users with clients who never used PCP (see Table 3) indicates that similar proportions of both males and females use PCP (32 percent); that proportionately more whites use it than other racial groups (42 percent of whites compared to 8 percent of blacks, 13 percent of American Indians, and 9 percent of Hispanics); that PCP use is more frequent in the suburbs (44.1 percent of all suburban clients compared with about 30 percent from urban and rural settings); that PCP users are slightly older at admission, with somewhat more years of education and have a higher Socio-Econcmic Status than users of other drugs.[1]

<u>Frequency of Use of</u> PCP. Among the 561 current users of PCP (see Table 4) approximately 50 percent were found to be using it at an average frequency of at least once per week during the three months prior to admission.

<u>The Onset of PCP</u> use. The man age of first PCP use was 14.6 years of age and the mean age of first continuous use was 14.8 years. Females reported the earlier mean age of first use for PCP: 14.4 years compared to 14.7 years for males. This finding is consistent with most other drug types in this study (except alcohol, marihuana, and inhalants).

In the comparison of age of first use of PCP across ethnic groups, American Indians were noted to have the earliest mean age of first use (13.89) closely followed by Hispanics (14.00). (The number of PCP users in these two groups, however,was too small to draw any inferences.) Whites reported the third earliest age of PCP use with a man of 14.58, and blacks were the oldest (15.25).

<u>Regional Distribution of</u> PCP Use. The National Youth Polydrug Study divided the United States into seven sampling regions. It should be stated that the sample was not stratified by region, which mans

TABLE 3

COMPARISON OF SUBJECTS WHO "EVER USED" WITH THOSE WHO "NEVER USED" PCP, ON DEMOGRAPHIC AND BACKGROUND CHARACTERISTICS

	used PCP	Did not use PCP	Total
sex			
Males	534 (31.9%)	1138 (68.1%)	1672 (100%)
Females	336 (31.6%)	725 (68.4%)	1061 (100%)
χ^2 = .02 (N.S.)			
dfs = 1			
Race			
White	784 (42)	1068 (58)	1852 (100%)
Black	33 (8)	354 (92)	387 (100%)
American Indian	18 (13)	116 (87)	134 (100%)
Hispanic	27 (9)	274 (91)	301 (100%)
χ^2 = 282.3			
dfs = 3			
$p<.0001$			
Residence			
Urban	544 (29.9)	1274 (70.1)	1818 (100%)
Suburban	194 (44.1)	246 (55.9)	440 (100%)
Rural and Small Town	131 (29.6)	312 (70.4)	643 (100%)
χ^2 = 34.2			
dfs = 5			
$p<.001$			

	$\tilde{x}$	S.D.	N	x	S.D.	N	t	p<
Age	16.2	1.4	875	15.8	1.3	1874	7.1	.001
Education	9.4	2.6	873	9.0	2.5	1853	3.7	.001
Socioeconomic status	45.4	13.8	875	41.0	15.1	1874	7.6	.001

TABLE 4

CURRENT FREQUENCY* OF PCP USE BY SUBJECTS CURRENTLY USING PCP

	N	%
Less than once a month	97	17.3
Once a month	69	12.3
Two to three times a month	112	20.0
Once a week	83	14.8
Two to three times a week	99	17.6
Four to six times a week	28	5.0
Daily	41	7.3
Twice a day	12	2.1
Three or more times a day	20	3.6
TOTAL	561	100.

* "Current" frequency is defined as the average frequency of use during three-month period before admission

the proportion of the youth population in treatment in each region was not a criterion for inclusion in the sample. It may be that certain states are overrepresented in proportion to their population, e.g., the relatively large number of cases in the sample from Illinois and Florida. Conversely, we know from the DAWN system that the San Francisco Bay area is one of the centers of PCP use, and is underrepresented in this sample.

The regional prevalence of PCP in the NYPS sample indicates that the Great Lakes and the Midwest regions show the highest rate of PCP use with 46.6 percent (N = 270) and 46.4 percent (N = 116) of each region's clients ever using PCP. Since the number of clients from these regions is fairly large and these clients were adimitted to 29 different treatment programs these data seem to be a valid representation of PCP use in these regions. They exceed the rates reported in DAWN and probably reflect the increased trend of PCP use among youth during the past two years. Other regions show PCP to be used by 31.5 percent of the clients from the Southeast (N = 153); by 27.2 percent of the clients from the West Coast; by 24.2 percent of clients from the Northeast; and by 23.8 percent of clients from the Southwest.

<u>The PCP User vs. the Nonuser.</u> Perhaps one of the most notable differences those who ever used PCP and those who did not is the greater involvement of the PCP users in polydrug abuse: PCP users reported using twice as many substances as the nonuser of PCP, with PCP users reporting a mean of 6.0 substances ever used (S.D. = 2.6), while nonusers of PCP reported a mean of 2.8 substances ever used (S.D. = 1.8), ($t = 33.4$, $p < .0001$). PCP users also reported a higher mean number of drugs used during the three months prior to admission to treatment: 5.8 substances (S.D. = 2.6) compared to a man of 2.6 substances (S.D. = 1.8) by nonusers of PCP ($t = 28.1$, $p < .0001$). Thus, for this youth population seeking treatment for drug abuse, PCP use is an integral part of a larger polydrug abuse problem that is more serious and complex than for the nonuser of PCP.

It is of particular interest that not a single subject who used PCP in this study used only this substance. All PCP users used other substances either at other times or concurrently with PCP. Almost all of them users used marihuana: 99.5 percent. other drugs reported used by PCP users were: alcohol (by 97.7 percent of PCP users); hashish (by 77.8 percent of PCP users): amphetamine (75.8 percent); hallucinogens (72.2 percent). Aside from alcohol and marihuana, which are almost universally used in this sample, and aside from hashish, PCP is next most often used by users of amphetamines and hallucinogens.

When looking at the use of multiple drugs from the other direction, we find that the users of other sedatives (61.7 percent), over-the-counter drugs (61.6 percent) and other opiates (61.1 percent) were most likely also to have ever used PCP.

A Profile of the PCP User

A correlational profile of the PCP user was developed from analysis in which PCP use was correlated with each of 33 demographic, social history, and background variables. A three points scale measure was utilized for PCP use, as follows: a score of 1 was assigned for no PCP use, a score of 2 for irregular PCP use, and a score of 3 for regular PCP use. Table 5 presents the list of the 18 variables (from among the 33) which had a bi-variate correlational value of + .10 or greater with PCP use. The profileof the PCP users (compared to the nonusers), which was derived from this analysis, is as follows, (listing the descriptors in rank order of magnitude of the correlation): (1) used regularly a greater number of different drugs; (2) white; (3) more often took more than one drug at a time (in combination) "to boost, balance or counteract the effects" of one drug; (4) became drunk from drinking alcohol more often; (5) had more arrests for substance related offenses; (6) were picked up more times by the police; (7) had more overdose episodes (OD's); (8) reported more obstacles to school attendance; (9) had more arrests for violent and weapons offenses; (10) listed more types of problems as reasons for contacting a treatment program; (11) more arrests for property offenses; (12) higher socio-economic status; (13) older; (14) adjudicated delinquent; (15) tended to reside in suburbia; (16) more often was admitted to treatment in hospitals and residential settings than to outpatient settings: (17) more often made suicidal attempts; and (18) less often were referred to treatment by peers.

Predicting "Regular" use of PCP. The variables employed in constructing the profile of the PCP users were also used to "predict" regular use of PCP. Clients were divided into two groups, regular PCP users (those using PCP at least once a week for a period of at least one month) and those who did not use PCP at all. Clients who had used PCP minimally, but never at a frequency of at least once per week for a period of one month, were excluded from this analysis. The analysis was composed of two steps: first, a bivariate correlation of all the variables includied in the analysis; second, a step-wise multiple regression in which the dependent variable is the regular use of PCP and the independent variables are a subset of the variables appearing in the correlation.

The bivariate correlation of the variables employed to predict regular PCP use showed that the strongest association of regular use of PCP is the number of substances regularly used ("Regsum"): r = .63. Since it seems reasonable to consider the relationship of demographic and other variables to PCP use separately from the question of how many other drugs the subject has used, we did not include this variable, "Regsum," in the equation of the step-wise multiple regression. The other background variables accounted for 16.8 percent of the variance in the differentiation of the regular PCP users from the nonusers (see Table 6). It might, thus, be said that it provides only one-sixth of the information that would be needed to "predict" accurately regular PCP use. The rank order of these variables, according to their relative abilities to "predict" to regular PCP use is as follows: (1) Race, (being white), accounts for 9.1 percent of the variance; (2) "the number of times

TABLE 5

CORRELATIONS OF CLIENT DESCRIPTORS WITH REGULAR USE OF PCP

	Correlation With Regular PCP Use
Number of drugs regularly used	.63
Race (white)	.31
Used more than one drug at a time	.31
Number of times became drunk	.22
Number of arrests for drug offenses	.19
Number of O.D.'s	.18
Number of times "picked up" by the poice	.18
Number of obstacles to school attendance	.17
Listed more types of problems as reasons for entering treatment	.16
Number of arrests for violent and weapons offenses	.16
Socioeconomic status	.14
Number of arrests for property offenses	.14
Age of admission	.12
Adjudicated delinquent	.12
Treatment program located in the suburbs	.11
Admitted to outpatient drug treatment program	-.11
Referred to treatment by peers	-.10
Number of suicide attempts	.10

TABLE 6

THE REGRESSION OF DEMOGRAPHIC AND OTHER HISTORY VARIABLES
ON REGULAR USE OF PCP
(STEP-WISE MULTIPLE REGRESSION PROGRAM)
(DEPENDENT CRITERION VARIABLE: REGULAR USE OF PCP)

Variable	Beta	Significance	Variance (R^2)	Simple
Race (1 = white; 0 = other)	.22	p = .0001	.091	.30
Frequency of Getting Drunk	.12	p = .0001	.025	.22
# of O.D.'s	.11	p = .0001	.02	.18
# of Obstacles to School Attendance	.12	p = .0001	.012	.17
Age	.08	p = .0001	.004	.12
Suburban (1 = from the suburbs 0 = other)	.06	p = .001	.004	.11
Referred by Peer	-.06	p = .002	.002	-.10
Socio Economic Status	.03	p= .20	.001	.13
Months Employed Last Two Years	.02	p = .21	.001	.11
Death of a Parental Figure	-.03	p = .13	.001	-.03
Intact Family Structure (0 = Intact; 1 = broken)	-.02	p = .20	.001	-.02
Sex	.02	p=.37	-	.00
# of Suicide Attempts	.01	p= .68	-	.09

the client got drunk" was the next variable in the equation, and added 2.5 percent to the explained variance, after controlling for race; (3) the number of OD's added 2.0 percent to the explained variance, after controlling for the two previously indicated variables; (4) "the number of obstacles to school attendance" added 1.2 percent to the explained variance, after controlling for the above-listed variables: (5) age added 1 percent; (6) suburban residence (versus living in an urban or rural location) added .4 percent.

The variables that did not enter into the equation to a statistically significant degree in explaining or predicting regular PCP use were sex, socioeconomic status, education, the number of months employed in the last two years, intactness of the family, and the number of suicide attempts. Some of these variables did not enter into the equation since they are significantly correlated with variables that had already been entered into the regression equation. For example, SES and employment are related to being white (race) and living in the suburbs (residence). Suicide attempts may have been excluded from the equation since they are correlated with OD's (r = .15). Education, which is highly related to age, was not included in the regression for the same reason. However, the sex variable was excluded from the regression equation because it was not associated with regular use of PCP; there is no difference between the sexes in their predisposition to be regular users OF PCP.

The PCP User in the NYPS-A Summary. The above review of PCP use in the NYPS indicates that the spread of this substance into the youth population occurs primarily among the white suburban population and that PCP has not as yet reached the same level of use within the inner city or among the underprivileged minorities. PCP is being added to an already existing pattern of multiple substance use and is not used by youth who do not use other drugs.

Two thirds of those young clients in the NYPS sample who ever tried PCP used it at least weekly. PCP is likely to be used by clients who have a previous history of treatment either for substance use or emotional problems. Self-destructive behavior is also much more prevalent among the PCP users as compared with nonusers of PCP. The PCP users were also found to have a more extensive involvement in the criminal justice system and more dysfunction in the education system. Lastly, the PCP users were found to be characterized by their low level of heroin use. Whether the dependence of adults on heroin is also associated with a lower prevalence of PCP, as found among youth, is yet to be determined.

Hospital-Based Youth Study

The authors conducted a study of 179 youthful (age 12 - 18 years) phencyclidine users seen at one county hospital in the San Francisco Oakland area between 1968 and 1976.

During the eight year period the majority of these patients (76.3

percent) were males, with a mean age of 16.8 years. The races represented were 96.1 percent Caucasian, 2.8 percent black and .6 percent Asian.

A large proportion of these patients were transported to the hospital by public transportation. The majority were brought to the emergency room by police vehicle (43.0 percent) or ambulance (31.8 percent). In most cases these patients were accompanied by police (39.1 percent), emergency service attendants (32.4 percent), perents (11.7 percent), friends (5.0 percent) and rarely by drug treament staff (2.8 percent).

Reasons for hospital contact were primarily treatment (75.4 percent), a medical check for juvenile hall (12.3 percent), public service evaluation (4.5 percent), or a medical check for police (3.9 percent). In most cases these phencyclidine users were retained for observation (43.6 percent), admitted to the emergency room (35.2 percent), or admitted to a service (2.2 percent). Only 16.8 pat-cent of these patients were immediately checked and released.

At the time of hospital contact, about half (49.2 percent) of the patients were disoriented, a third (31.8 percent) were uncooperative, and a quarter (26.8 percent) were either awake with decreased consciousness or were stuporous or comatose.

The majority of these patients (80.4 percent) had taken only phencyclidine prior to hospital presentation. The most popular substance taken in combination with phencyclidine was alcohol (15.1 percent), followed by barbiturates (1.1 percent).

Among this youthful population, a quarter (24.0 percent) were chronic users of phencyclidine. These patients qualified as chronic users by having taken phencyclidine on a regular basis for greater than a six month period with multiple hospital admissions for phencyclidine-related problems. The youngest chronic user was a 15-year-old female.

Similarities in Drug Study Findings

A number of consistent patterns appear from an analysis of the data from the DAWN, NYPS, and the authors studies' on phencyclidine.

There is an overrepresentation of Caucasians among phencyclidine users, accounting for more than 90 percent of all identified patients. This trend is observed in all of the major data sources. However, it should be noted that in certain geographic areas phencyclidine use appears to be limited to other specific groups, such as blacks (Washington, D.C., Watts) and Mexican Americans (San Jose).

The majority of the individuals report the "psychic effects" as their primary reason for continued use of phencyclidine. Among all individuals exposed to this drug, approximately 23 percent become chronic users. Males represent the highest number of chronic users as well as hospital emergency room contacts for problems related to phencyclidine.

Phencyclidine users utilize and apparently need more medical treatmentservices than other drug users.

Problems Seen Where Phencyclidine is Continuously Available

As the availability of phencyclidine increases in a commnity, there is a direct relationship with the number of emergency room contacts and community problems such as driving under the influence and violent and bizarre behavior - behavioral toxicity.

In San Jose, California, the police department has gathered data on seizures of phencyclidine for the past three years. During the first quarter of 1975 (January - March), 69.7 grams of phencyclidine were confiscated. The following year during the same period, 125.1 grams of illegal material were collected. For the first quarter of 1977, 3,951 grams of phencyclidine have been recovered.

In 1976 for the first quarter there were 69 patients treated for phencyclidine-related problems; in 1977, 100 patients were seen during this same period.

New problems have surfaced in communities (Alameda, Santa Clara, and Los Angeles) in direct proportion to the frequency and regularity of phencyclidine abuse. Violent and bizarre behavior is seen in the home, in public places, and in schools, often disrupting education. Young people exhibit unexplained speech problems, menory loss, thinking disorders, personality changes, anxiety, severe depression, and suicidal and homicidal tendencies.

An increasing number of young people appearing violent, bizarre, unresponsive, extremely confused, or acutely psychotic are being seen in local emergency rooms. With increased use of phencyclidine, an upsurge in violent crimes that culminate in homicide is observed.

Police report erratic driving and inappropriate behavior following automobile accidents in individuals who have no apparent evidence of alcohol or sedative hypnotic ingestion. On toxicological examination only the isolated presence of phencyclidine is often discovered.

Young people who are observed to be highly intoxicated in public are often arrested for sale, possession, and being under the influence of phencyclidine. In addition, an increasing number of referrals by family, friends, and the criminal justice system are made to community drug abuse programs in an effort to deal with this new drug problem.

The following are typical cases that illustrate the problems seen in youth on phencyclidine.

CASE 1

A 15-year-old Caucasian male with no clothes on was found by police in a field, hanging on to a barbed wire fence. He was disoriented and incoherent upon questioning. A physical examination revealed a confused, disoriented youth with inflamed eyes, bloody mouth with an upper incisor missing, multiple scratches of the trunk, and scratches and lacerations of extremities. Fluctuations in orientation were observed over the next seven hours ranging from cooperative and alert to unrousable. Prior to being discharged the patient stated that he had "smoked some phencyclidine and got awfully stoned."

CASE 2

A 17-year old Caucasian male arrested by police had allegedly ingested several phencyclidine joints, and over a 1 hour 45 minute period became progressively uncommunicative and withdrawn. The youth was transported from jail to a local emergency room. On admission he was observed lying quietly, eyes wide open, with a broad smile on his face. Although responsive to commands, he was only able to mouth words rather than speak. When given ipecac, he vomited green parsley flakes. Over the next six hours he alternated between quietly staring at the ceiling and being abusive, agitated, combative, and fighting restraints. Upon regaining normal orientation, he was observed for two additional hours and released.

CASE 3

An 18-year old Caucasian male ingested tablets and capsules in his possession prior to a police traffic stop. Immediately after the officers departed he was driven to an apartment where the other occupants of the automobile induced vomiting of what they believed was all of the ingested material. Later he began screaming and having convulsions. He was driven to a local hospital where he was pronounced dead on arrival. The coroner ruled that death was caused by aspiration of gastric contents due to phencyclidine ingestion. Phencyclidine (urine level of 0.5 mg/ml) was the only drug found on toxicological examination.

CASE 4

A 15-year old Caucasian male reported to be "out of hand" was seen at a local medical center for bizarre behavior. He had been involved with drugs and talked about "getting it all over." Later that month, he was found hanging by an electrical cord from a beam in his garage. Toxicological examination revealed a phencyclidine blood level of 0.10 mg/ml. No other drugs were detected.

CASE 5

During the summer a youth gave a pool party while his parents were away on vacation. A 17-year old Caucasian female guest was discoveredatthe bottom of the swimming pool. Post mortem examination revealed no head or neck trauma and the isolated presence of phencyclidine in the urine (0.5 mg/ml).

CASE 6

Distressed over a college setback, a 17-year old Caucasian male snorted phencyclidine for the first time, with friends. He lost consciousness, becoming apneic and cyanotic. On admission to the emergency room this semiconscious patient was agitated, had writhing movements of all extremities, vomited, and had copious nasal and oral secretions. Within three hours he appeared alert; three hours later he was cooperative and completely oriented.

CASE 7

A 16-year old Caucasian female smoked "a crystal joint" while at school and began acting bizarre. School authorities notified her mother who brought her to a local hospital. On admission she was dazed and unable to recall who gave her the drug or how much she had taken. The patient was oriented to person and place. A blood sample taken on admission was negative for sedative hypnotics. Urine obtained at the same time for toxicology was positive only for phencyclidine, with a value of 0.5 mg/ml. The patient became fully oriented 2 1/2 hours later and was discharged.

Case 8

A 16-year old male, acting belligerent and combative, was brought to the hospital from a party where he had smoked "crystal" and drunk beer. On admission he was drowsy but responsive to verbal stimuli. There were abrasions on his right arm and face. Over the next three hours he became verbally abusive, belligerent, and uncooperative and was transferred to the county hospital. Initially violent, he alternated between periods of sleep and moaning. Toxicology screen obtained at this time revealed a phencyclidine urine value of 1.1 mg/ml. Over the next 15 1/2 hours the patient became alert and oriented and was subsequently discharged.

Homicides

In addition to hospital presentations for complications related to phencyclidine intoxication, recently there have been several homicides committed by youth in which phencyclidine was implicated (San Jose and Los Angeles, California; Las Vegas, Nevada; Kansas City, Kansas). The defense attorneys in the majority of cases claim that their clients were not guilty either by reason of diminished capacity or of insanity (drug-induced psychosis). With defendants showing bizarre and violent behavior and sometimes defendants claiming amnesia to the event, (given the unique properties of phencyclidine) and the circumstances of many of these homicides, it appears that the legal issues raised will require much further debate and study.

Deaths

A large number of deaths have occurred in association with phencyclidine intoxication. In the majority of cases the immediate cause of death was asphyxia by drowning, or trauma, circumstantial evidence suggesting that death was secondary to the "behavioral toxicity" of phencyclidine. The user could not indicate where his limbs were in relation to three dimensional space or could not respond appropriately to imminent danger.

Other individuals have been found dead without apparent cause, the presence of phencyclidine in high concentrations constituting the only positive finding. The most probable cause of death in high dose phencyclidine intoxication is primary respiratory depression.

Phencyclidine users report going swimming while intoxicated because they experience an unusual but pleasant sensation from the water. Sensory disturbances, incoordination, and muscle rigidity resulting from "street" doses of phencyclidine may seriously interfere with the user's ability to swim, drive, climb at heights, flee from a fire, or sense imminent danger.

Suicide by self-inflicted trauma or a massive oral overdose of phencyclidine has occurred in the chronic user who became moody or severely depressed. It is the chronic user who is in possession of large amounts of phencyclidine. Threatening behavior or violence has resulted in provoked homicide.

Blood levels of phencyclidine as low as 100 mg/ml may be associated with behavioral effects leading to death by injury or trauma. Levels greater than 1.0 mg/ml are associated in most individuals with coma and may result in death secondary to medical complications or respiratory depression and seizures. Doses of 2.0 to 2.5 mg/ml and greater are probably uniformly fatal, producing primary respiratory depression and seizures.

Phencyclidine deaths nationally appear to be on the increase. In Los Angeles alone the Coroner's Office reported 26 phencyclidine-related deaths during 1977.

CHRONIC PHENCYCLIDINE USE

Phencyclidine became available on the illicit market in 1965 and initially was taken orally in the form of tablets and capsules. Around 1972, it became available primarily in the form of a leaf mixture in California, with crystalline phencyclidine sprinkled on parsley, mint, or marihuana and sold as "joints."

After experimenting with phencyclidine, increasing numbers of young people began using it on a regular basis. This trend peaked around 1972 and subsequently declined until 1974 when the incidence of phencyclidine abuse again rose. Where phencyclidine became continuously available, it gained a preferred drug status with several "cluster" groups who smoked it on a regular daily basis in Northern and Southern California. Chronic use of phencyclidine was first reported in 1972.

Chronic User Study

A study designed to describe chronic phencyclidine use patterns and determine evidence of chronic toxicity was carried out by the authors in the San Francisco Bay Area in February 1975. Individuals who had been treated for phencyclidine "overdose" at various music concerts were invited to participate. They in turn brought other known phencyclidine users into the study and in particular friends who had used large amounts over the longest period of time.

The final study group of twenty had used phencyclidine regularly (3 or more days per week) over a period greater than six months without concurrent, heavy use of other drugs. Phencyclidine was present in the urine samples obtained on both the initial and followup visits.

The 15 male and 5 female chronic users ranged in age from 20 - 43 years old with a mean age of 25. All were Caucasian. Eighteen (90 percent) were single and 19 (95 percent) had a heterosexual preference.

Patterns of Use

The mean age at first use was 19.2 years, with half the group (10) individuals 18 years old or younger. The majority (80 percent) had first used phencyclidine between 1967 and 1970 at 15 to 21 years of age, with a second group (20 percent) starting in 1972 and 1973.

Most users were introduced to phencyclidine by friends (85 percent) in a social setting, and took the drug out of curiosity (55 percent) or to get "high" (45 percent). Within one year, half were using phencyclidine regularly 3 or more times per week; by three years, 75 percent used phencyclidine regularly.

The cumulative period of regular use from first exposure to the time of the study ranged from 6 months to 5 1/2 years, with a mean of 27 1/2 months. The longest period of daily or almost daily (5 or more days per week) use averaged 10.3 months and the maximum period of abstinence averaged 5.9 months. The period of recent uninterrupted use of phencyclidine prior to the study averaged 9.9 months. Two to four times per month, users would go on 2 - 3 day "runs," taking phencyclidine repeatedly without sleeping. Seventy percent continued to use marihuana and 50 percent used alcohol on a regular basis during their use of phencyclidine.

By 1972 the availability on the illicit market of nearly pure phencyclidine in amounts of 1 gram or more allowed the individual to prepare joints for smoking of chosen strength, guarantee a long term or continual supply for the user. With possession of large amounts of phencyclidine, users started taking the drug on a regular basis.

The razor shavings from the "rock" crystal or the powder is sprinkled on parsley and smoked in the form of a joint. The amount of street-purchased material used in the preparation of one joint varies from 50 mg for a "street" joint to about 100 mg for a "regular" or "good" joint. Up to 1/4 gram was used in a "killer-diller," "heavy" or "party joint," which is often shared by many people.

The primary mode of taking phencyclidine was by smoking (90 percent) or snorting (10 percent) the drug. All the chronic users had taken phencyclidine at least once by smoking. The majority had also snorted phencyclidine (75 percent) and taken it by mouth (60 percent). Only 6 (30 percent) individuals had used phencyclidine intravenously. Five out of the 6 used. it intravenously not more than five times.

Smokers reported using the equivalent of 1 to 2 street joints or about 80 mg of street-purchased material 2 to 3 times per day. The average daily intake was about 216 mg by smoking. The reported maximum amounts used in a 24 hour period ranged from 1/4 to 1 gram and averaged 500 mg . The two individuals who regularly snorted phencyclidine estimated the 2 "lines" dose to be about 5 mg of street-purchased material. They would snort the drug 4 to 6 times per day. Toward the end of a prolonged period of daily use of phencyclidine, these 2 individuals would place amounts of up to 1/4 of a gram of powder (layered with parsley or as a crystal) in a pipe, and smoke it in one sitting.

Phencyclidine users reported that the subjective effects "come on" within 1 to 5 minutes of smoking a typical "street" joint and reach a "peak or a plateau" over a 5 to 30 minute period. They report staying "loaded" or "high" for 4 to 6 hours, followed by the "come down" which lasts 6 to 24 hours after taking the drug. Following a 2 - 3 day "run," the time before the user felt normal again was approximately 48 hours to one week. A more rapid onset of 30 seconds to 1 minute followed insufflation of a street dose in powdered form. The time course of the subjective effects otherwise did not appear to differ.

The Phencyclidine Experience and Why It Is Repeated

Eighty percent of the chronic users considered their first phencyclidine experience to be pleasantandwanted to take the drug again. They found it "fun," "exhilarating," and felt "happy" or "euphoric." It seemed to be a "perfect escape" or "a dream world."

Fifteen percent disliked their first experience feeling "scared" or finding it "terrible," while one individual (5 percent) characterized the experience as "strange," "weird, but interesting."

In 95 percent of the cases, first use occurred in a social setting, with 70 percent smoking and sharing a joint at a party or with a small group of friends (mean of 5) at someone's house. Four users (20 percent) related minor injuries, repeated vomiting, or arrests by the police as problems occurring with the first use. Three of these individuals had either snorted phencyclidine or taken it by mouth.

The phencyclidine "high" was reported to be very intense, several times stronger than marihuana, comparable to LSD, although shorter in duration. Most individuals compared it with LSD, but insisted that it was different, "in a class by itself."

The drug had a pronounced effect on the subjects' thinking, time perception, sense of reality, and mood. Thinking was described as "speeded" or "wired," the mind going faster while time was slowed down, with "no more reality." Everything was reported as being different, in another dimension, and seen from a new point of view. Life was dramatized, a fantasy world where "you don't have to dream, your wishes are fulfilled" and "what you want to happen comes true."

Everything was felt to be complete and make more sense. The mind could focus on one object and see beauty in the smallest thing. A sense of commnunity, oneness with others and with animals was reported. Religious thoughts and the experience of death were frequently mentioned. Mood states were also intensified, with users in most cases feeling happy or euphoric, although everyone had also experienced severe depression and had recognized the drug's potential for bringing one to either "the heights or the depths of being." Music was "absorbed" light was "felt," and space and depth were "distorted," "seen in 2D." Frequently users reported feeling like they were "floating." Rarely did they relate visual hallucinations.

Users also experienced a feeling of strength and endurance. They described feeling "powerful," "superior," "arrogant," with "bursts of energy," "like God was with you, and you could move mountains." There was also a loss of inhibitions. It was felt to be difficult to do things; one had "to think about moving or talking." In addition, they described feeling restless and nervous.

Chronic use of phencyclidine also took place in a social setting with the sharing of joints. Individuals would join in with 2 to 5 others at a friend's house or at home. The membership of a group who shared in the use of phencyclidine remained quite stable over long periods of regular use. They would listen to music, talk, dame, and enjoy sex together while "high." Less often they would go to a rock concert or go out in public. They took phencyclidine as frequently during the daytime as in the evening.

The majority (60 percent) continued to use phencyclidine because they enjoyed or liked the "high." Frequently all their friends used phencyclidine and "it had become a life style." At times the availability of phencyclidine or making money from phencyclidine sales played a role. For 80 percent of the users, phencyclidine was their drug of choice. Three individuals preferred heroin and one preferred seconal. Nonavailability, incarceration, or hospitalization were the major factors interrupting the regular use of phencyclidine. Participation in a drug treatment program or moving out of the area also interrupted the pattern of phencyclidine use.

Tolerance, Psychological Dependence, and Side Effects

Tolerance to the psychic effects of phencyclidine was reported by chronic users. Initially they would get "high" after 2 or 3 puffs on a phenyclidine joint; following a one week period of daily use they required 1/2 to 1 joint. After smoking for a period of 2 to 6 weeks, most individuals used 1 or 2 joints at a time. Some users reported being able to smoke up to 1/4 gram of street-purchased material at one sitting, following several months of regular, daily use. Psychological dependence, described as craving, was noted by chronic users, but no withdral symptoms were reported.

Phencyclidine taken in typical "street" doses was reported to prevent sleep for 8 to 12 hours, decrease appetite, and to cause constipation and urinary hesitancy. Chronic users averaged one meal or less per day and lost 10 to 35 pounds during periods of regular use.

Chronic Toxicity

Chronic phencyclidine users reported persistent problems with memory and speech, and difficulty with thinking following long periods of regular use of the drug. Recent memory capability appears to be primarily affected. Users complain of stuttering, inability to speak or blocking, and difficulty with articulation. Speech and memory difficulties lasted as long as 6 months to 1 year following prolonged daily use of large doses of phencyclidine.

Several chronic users complained of anxiety or nervousness during and following periods of regular phencyclidine use and sought psychiatric care. Some individuals became severely depressed, and attempted suicide on repeated occasions after chronic exposure to phencyclidine.

Chronic users reported personality change, social withdrawal, social isolation, and divorce resulting from their use of phencyclidine. In some cases, violent behavior was one of the effects.

Employment has been lost and education disrupted as a result of the effects of phencyclidine with chronic patterns of use. Frequent arrests for being under the influence of phencyclidine or for possession result in a criminal status.

Chronic phencyclidine use has culminated in a picture of violent and aggressive behavior, paranoia, delusional thinking, and auditory hallucinations. In most cases no known behavioral disturbance or psychiatric problems preceded the use of phencyclidine. Typically, the individual had used phencyclidine over several months or a few years with the same group of friends. Form apparent reason a sudden development of paranoia and auditory hallucinations was accompanied by violent, unpredictable behavior. Friends and family often became fearful and brought the user to medical attention.

Laboratory and Neurological Findings

Fourteen (70 percent) individuals reported using phencyclidine within 24 hours of the clinical examination and 85 percent within 48 hours (see Table 7). All mine samples obtained just prior to the physical examination were found to contain detectable levels of unchanged phencyclidine by gas chromatography-mass spectrometry and the majority of serum samples (85 percent) obtained were also positive for phencyclidine. Phencyclidine levels were higher in cases where the last use of phencyclidine by history was within a 48 hour period (see Table 8).

Eight (40 percent) individuals reported using phencyclidine within 6 hours of the examination and had a "blank stare" appearance and slurred speech. Ptosis, conjunctival infection, and vertical and horizontal nystagmus were present. They had an ataxic gait and were unable to tandem walk. One third appeared lethargic and were disoriented for time and place.

Individuals reporting no phencyclidine use for 24 to 48 hours prior to the examination had unsustained vertical and horizontal nystagmus and difficulty with tandem gait (see Chart A).

On electroencephalographic study, one chronic user showed bursts of spike and slow wave activity associated with observed myoclonic twitching in response to photo-stimulation (see Photograph A). Three chronic users selected for electroocculographic study showed jerk nystagmus, saccadic pursuit, and hypometric slowed saccades (see Photographs B,C,D). Urine samples concurrent with test procedures were positive for phencyclidine.

TABLE 7

HISTORY OF PCP USE PRIOR TO PHYSICAL EXAMINATION

LAST USE	NO. CASES	CUMULATIVE PERCENTAGE
< 6 hours	7	35.0
7 - 24 hours	7	70.0
25 - 48 hours	3	85.0
49 - 72 hours	1	90.0
97 -120 hours	2	100.0

TABLE 8

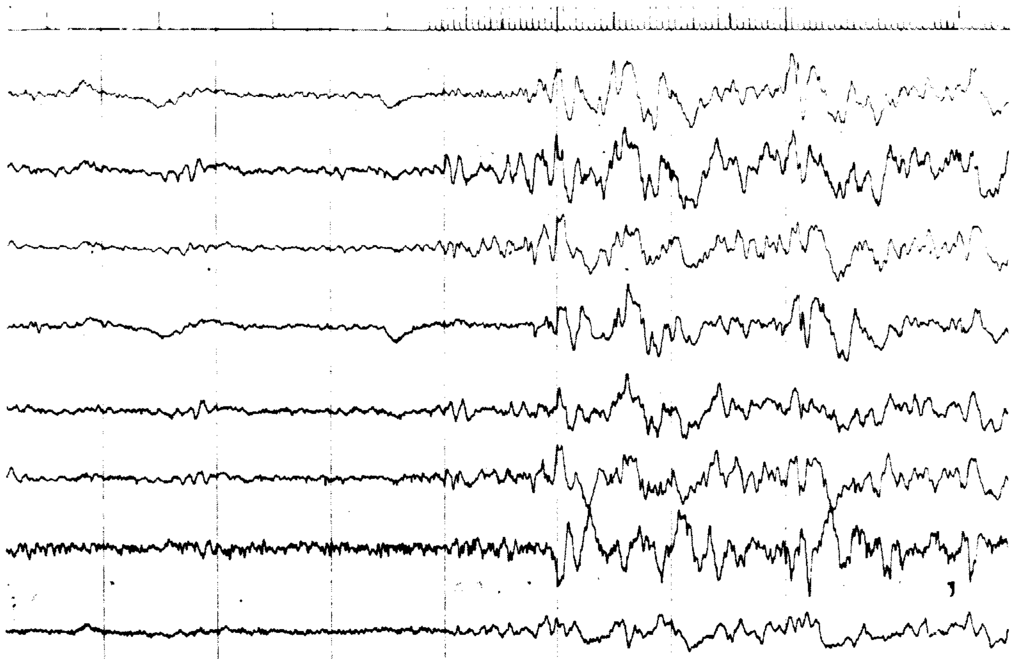
CHRONIC USERS' URINES COLLECTED PRIOR TO P.E.

LAST USE	NO. CASES	URINE LEVEL
1 - 12 hours	8	1.73 ug/ml
13 - 24 hours	4	0.85 ug/ml
25 - 48 hours	4	1.24 ug/ml
> 48 hours	4	0.13 ug/ml

Chart A
Physical Examination Findings

Vital Signs	<6 hours	7 - 24 hours	25 -48 hours	>48 hours
B.P. - SYST.	132	132	115	109
- DIAST.	79	71	65	65
PULSE	88	79	78	72
RESPIR. RATE	15	17	14	16
ALTERED STATE OF CONSCIOUSNESS (Lethargic, somnolent, 'high'_	+	-	-	-
Disorientation (time, place)	+	-	-	-
SPECH (slow, slurred,) repetitive, inter- mittently unable)	+	+	-	-
E.O.M.M.				
'Stare' appearance	+	+	-	-
Disconjugate gaze	+	+	-	-
Nystagmus				
H	+	+	+	+
V	+	+	+	+
Sustained	+	-	-	-
PUPILS				
Size				
Light Reaction (Sluggish, decreased amplitude)	+	+	-	-
Corneal reflex (Decreased or absent)	+	+	-	-
MOTOR SYSTEM				
Movements:				
Repetitive	+	+	-	-
Restlessness	+			
Catalepsy	+	-	-	-
Rigidity	+	+	-	-
Hyperreflexia (L/e)	+	+	-	-
Gait (Ataxic, broad based)	+	+	-	-
COORDINATION				
Tandem standing (Difficulty or unable)	+	+	+	-

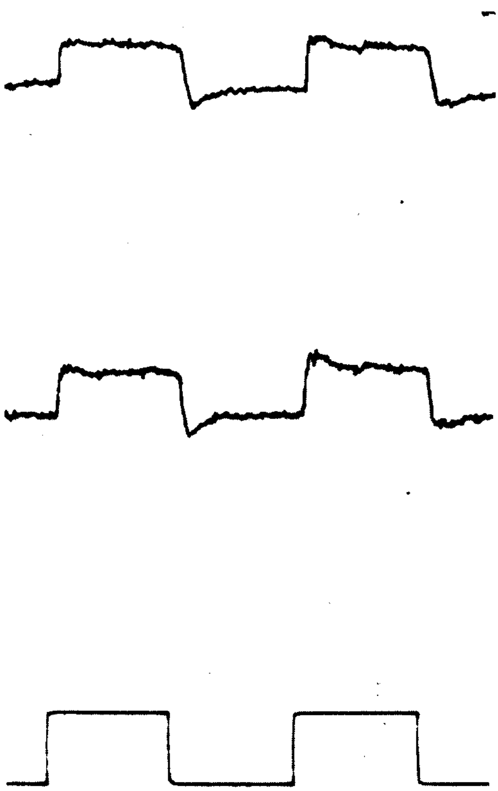
Photograph A
Chronic Phencyclidine User Electroencephalogram



This abnormal electroencephalogram shows a positive photoconvulsive response. Intermittent pkotic stimulation at botk Slow and fast flash frequencies induces bursts of spike and slow wave activity. With sustained 20 cycles per second stimulation, involuntary myoclonic twitching is noticed on the left face, arm and leg. This recurs with repeat pkotic stimulation, and is again clinically focalized to the Zeft side, although electroencephalographically bilateral spike and slow wave discharges occur.

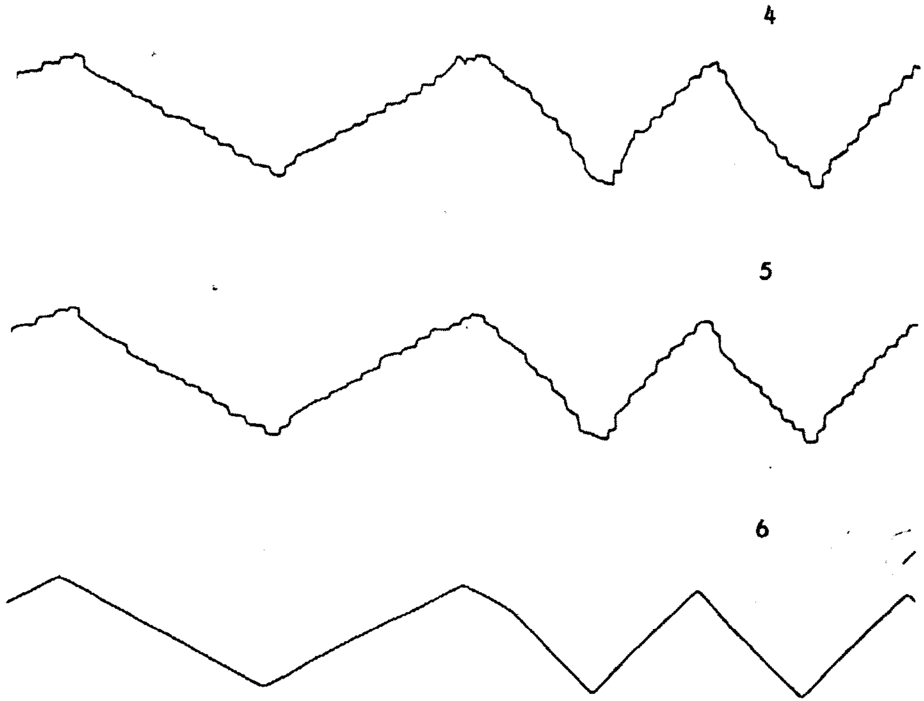
Photograph B
PCP-Induced Oculomotor Disorders

These records were obtained from photoelectric cells placed about each eye in the horizontal plane and then from EOG electrodes placed about each eye in the vertical plane.



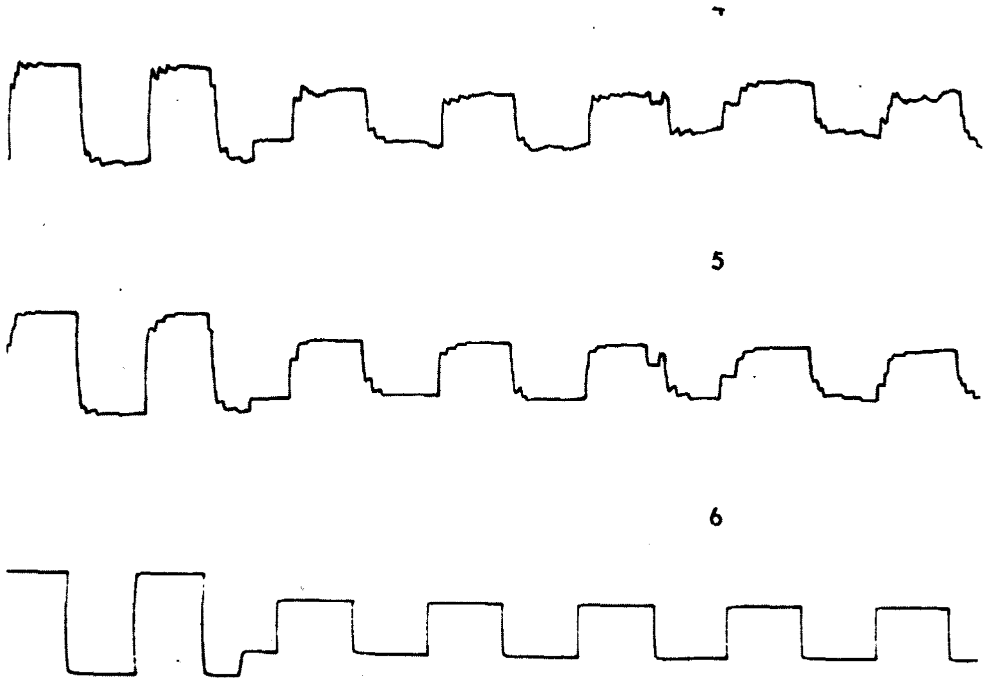
FIXATION: *Jerk nystagmus at the gaze limit of the photocell technique, 15°.*

Photograph C



SMOOTH PURSUIT: *Ramp pursuit grossly saccadic (staircase) in horizontal and vertical planes.*

Photograph D



SACCADES: *Grossly abnormal horizontal and vertical hypometric Slowed* saccades.

THE ACUTE STATES OF PHENCYCLIDINE INTOXICATION

History and Presentation

The spectrum of signs and symptoms and the pattern of recovery in acute intoxication with phencyclidine vary with the dose and route of administration

Individuals are most frequently brought to a hospital emergency room when found unresponsive or when exhibiting bizarre or violent behavior (see Table 9). Others are brought in after having been cbserved to be grossly incoordinated, driving erratically, or acting inappropriately after an automobile accident. Some individuals present with minor or major trauma.

Clinical Picture and Course

A confusional state delirium lasting less than 8 hours appears to follow a typical street dose after smoking one "joint." Individuals who either smoke greater amounts or take a higher dose orally or by "snorting" may present in stupor or coma. This initial state lasts less thanthreehours in most cases and a confusional dose-related state follows for 24 to 72 hours. Massive oral "overdose" involving up to one gram of street-purchased material has resulted in periods of stupor or coma of several hours to two weeks in duration. This initial stage is followed by a prolonged recovery with a confusional state persisting up to two weeks (see Table 10).

The confusional state delirium induced by phencyclidine is characterized by immobility and a "blank stare" appearance in a-patient who is noncommunicative. The patient is disoriented and apprehensive, becoming easily agitated or excited. These patients are grossly ataxic and exhibit horizontal and vertical nystagmus and catalepsy on testing. Muscle rigidity may be present. Most patients are communicative within 1 - 2 hours, and appear alert, oriented, and exhibit normal behavior within 5 hours of admission to the emergency room.

In phencyclidine stupor or coma, the eyes may remain open although the patient is responsive only to deep pain. Hypertension and tachycardia are present, and in all but the more massive oral "overdoses" respiration is normal. The pupils are initially miotic but reactive to light. Spontaneous nystagmus, 'purposeless" movements, facial grimacing, and muscle rigidity on stimulation are characteristic findings. Repeated episodes of vomiting, increased bronchial and oral secretions, and profuse diaphoresis are frequently observed. An initial stage of stupor or coma lasting less than four hours my be followed by a period of confusion or delirium lasting up to 2 1/2 days (refer to Table 11).

TABLE 9

PRESENTING PICTURE AMONG 18 CASES
OF ACUTE PHENCYCLIDINE INTOXICATION

PRESENTING PICTURE	CASES	PERCENT
Unresponsive	11	61.0
Bizzaare behavior	4	22.0
Automobile accident	2	11.0
Violent behavior	1	6.0

TABLE 10

COURSE OF RECOVERY OF 16 INDIVIDUALS
BY STATE OF CONSCIOUSNESS ON ADMISSION

PRESENTATION	CASES	DURATION OF INITIAL STATE	PERIOD OF DELIRIUM OR CONFUSION	TIME REQUIRED UNTIL "NORMAL"
Group I: Confusional state and history of smoking 1 street joint	4	5 hours (3-8 hours)	------	5 hours (3-8 hours)
Group II: Initial state of stupor or coma	6	3 hours (1-4 hours)	34 hours (5-62 hours)	37 hours (14-66 hours)
GROUP III: Initial state of stupor or coma (> 6 hours	4	50 hours (6-103 hours)	163 hours (75-288 hours)	212 hours (114-360 hours)

TABLE 11

SUMMARY OF CLINICAL HISTORIES OF 18 CASES OF ACUTE PHENCYCLIDINE INTOXICATION

	ACUTE CONFUSIONAL STATE OR DELIRIUM (N=7)	STUPOR OR COMA (N=11)
PART I: <u>VITAL SIGNS</u>		
A. Respiratory rate (normal or) slightly increased	24 mean	21 mean
B. Blood pressure (increased)	18-32 mean	16-25 mean
Systolic	142 mean 116-160 range	155 mean 100-180 range
Diastolic	85 mean 76-100 range	94 mean 60-110 range
C. Pulse (increased)	105 mean 88-140 range	88 mean 60-112 range
D. Temperature (normal or slightly increased)	100.1°F 98.8°-101.4°F range	99.3°F 97.0°-100.8°F range
PART II: <u>CLINICAL FEATURES</u>		
A. Responsiveness	Appears awake; initially uncommunicative, may respond to commands or respond to simple questions with nodding or eye movement later incomplete verbal responses and then becomes communicative/talkative	Unresponsive to verbal stimuli, responds with movement to deep pain

TABLE 11 (Continued)

	ACUTE CONFUSIONAL STATE OR DELIRIUM (N=7)	STUPOR OR COMA (N=11)
B. Orientation	Disoriented for time and place; appears confused and fearful; amnesia for episode	—
C. Behavior	Agitated, excited, combative; regressive; self-destructive or "bizarre" behavior; insomnia, anorexia, incontinence; followed by depression, irritability and emotional lability	—
D. Speech	Dysarthria (slurred), perseveration; may be intermittently anarthric	Vocalizations; "moaning," "groaning," "grunting;" followed by anarthria and dysfluency, initially with automatic speech
<u>EYE SIGNS</u>		
A. Eye lids	Eyes open ("stare" appearance) with ptosis	Eyes open ("awake" appearance) or eyes closed
B. Eye position & movements	Paucity of spontaneous eye movements appearance, may be fixation instability dysconjugate gaze or hypometric saccadest	May be roving eye movements; dysconjugate gaze; doll's eye movements present
C. Nystagmus	Bilateral horizontal jerk nystagmus; may be vertical nystagmus (upward-downward)	Interittent horizontal and vertical nystagmus at rest

TABLE 11 (continued)

	ACUTE CONFUSIONAL STATE OR DELIRIUM (N=7)	STUPOR OR COMA (N=11)
D. Corneal reflex	Decreased or absent	Decreased or absent
<u>MOTOR SYSTEM</u>		
A. Gait	Grossly ataxic (sensory), unable to tandem stand/walk; may be component of muscle rigidity	————
B. Muscle tone	Rigidity (catatonia), catalepsy (waxy rigidity)	Muscle rigidity, on stimulation, opisthotonic posturing, decerebrate rigidity
C. Movements	Motor restlessness, repetitive movements, facial grimacing	Spontaneous "purposeless movement;" muscle tremor, muscle twitching, fasiculations
D. DTR's	Increased	Increased
E. Seizure activity	————	Generalized motor seizures may be early or delayed in appearance and repetitive
<u>OTHER</u>		
A. Vomiting (central)	Repeated episodes over 1/2 to 3 hours period	Repeated episodes

TABLE 11 (continued)

	ACUTE CONFUSIONAL STATE OR DELIRIUM (N=7)	STUPOR OR COMA (N=11)
B. Increased secretions (lacrimation, salivation, diaphoresis, bronchorrhea)	"Drooling," diaphoretic	Secretions in posterior pharnys at nares and mouth; tearing, diaphoresis
C. Evidence of minor trauma	Abrasions, lacerations, ecchymoses	Abrasions, lacerations, ecchymoses

Urine phencyclidine levels of 26.2 - 151.9 mg/ml were found in samples collected within 12 hours of admission in four patients who remained in coma for greater than 6 hours and required between 7- 15 days for recovery to normal (see Table 12).

Status epilepticus followed by cardiopulmonary arrest without recovery has been reported with a blood phencyclidine level of 7.0 mg/ml.

Diagnosis

Drug use is frequently considered to be the etiology of symptoms when a young person presents acutely confused or delirious with no focal neurological findings. But encephalitis, head injury, postictal state, and metabolic causes must be ruled out.

The "blank-stare" appearance and catatonia-catalepsy appear to be unique to phencyclidine as effects of commonly abused drugs. The absence of mydriases, and the presence of ataxia and nystagmus rule out the central nervous system stimulants and LSD when considering the acutely excited and confused patient.

In coma with or without respiratory depression, hypertension and hyperreflexia differentiate phencyclidine intoxication from a sedative hypnotic "overdose." If, in addition, decerebrate posturing or repetitive generalized seizure activity is observed phencyclidine intoxication should be suspected, although other serious causes producing a similar clinical picture must be ruled out.

Cases involving the ingestion of large doses of phencyclidine present with coma which may last several hours or days. The prolonged recovery with a confusional state lasting up to two weeks is characteristic of phencyclidine intoxication. If persistent paranoid or depressive psychosis follows recovery, phencyclidine intoxication should be suspects.

In combined intoxications involving phencyclidine and barbiturates, normal or low blood pressure, hyperreflexia and respiratory depression may be observed.

Management

The acutely confused patient is best managed by sensory isolation with observation at a distance. Minimizing verbal and tactile stimulation does not preclude the monitoring of vital signs. Important functions to monitor are respiration, blood pressure, muscle tone and activity, renal function, and temperature. Ideally, the patient would be placed on a cushioned floor in a "quiet room" with a monitor present. In most settings, protection of the patient and staff necessitates the use of restraints.

The early management of the stuporous or comatose patient involves gastric aspiration-lavage and nasopharyngeal suctioning. In view

TABLE 12

CLINICAL HISTORIES OF TWO CASES OF ACUTE PHENCYCLIDINE INTOXICATION

	CASE 1	CASE 2
Age	22	22
Sex	Male	Male
Estimated dose	One gram "street" material	One gram+ "street" material
Route	by mouth	By mouth
Coma	25 hours	103 hours
Confusion delirium and somnolence	71 hours	77 hours
Depression, irritability and emotional lability	84+ hours	32 hours
alert and oriented	Transferred to psychiatric unit	178 hours
Cardiovascular system		
blood pressure (mean)	147/92 (84 hours)	151/98 (108 hours)
pulse (mean)	94	111
Repiratory status	Excessive mucous/secretions on admission; hypoventilation x15 ours, Tidal; volume 100 cc's; irregular respira-tions with 5 sec. periods of apnea x15 ours; required ventilatory assistance x27 hours; complications; right upper lobe pneumonitis	Excessive Mucous/secretions, hypoventilation on admission; hypoventilation x60 hours, Tidal; Volume 50 cc's; apnea x4 hours; required ventilatory assistance x107 hours; compli-cations: bilateral basilar pneumonitis
Seizure and motor activity	Decerabrate rigidity; opisthotonic posturing; muscle tremors, twitching; generalized motor seizures at 66 and 78 hours; treatment: Valium and Dilantin	Decerbrate rigidity; opisthotonic posturing; muscle tremors; twitching; focal motor seizures at 3 and 21 hours; generalized motor seizures at 3-1/2 & 89 hours; treatment: Dilantin
Toxicology	On admission: 26.2 µg/ml PCP (urine)	On admission: 151.9 µg/ml PCP (urine)
Day 1	26.2 µg/ml	151.9 µg/ml
2	18.2 µg/ml	
3	15.9 µg/ml; 18.0 µg/ml 18.5 µg/ml; 20.0 µg/ml	
4	4.7 µg/ml; 1.3 µg/ml 0.5 µg/ml;	
5	1.2 µg/ml; 0.1 µg/ml	
6	0.4 µg/ml; 0.3 µg/ml	

of the recovery of large amounts of phencyclidine from the stomach contents in fatal "overdoses," gastric lavage is indicated in oral ingestions.

Intubation is often difficult because of increased muscle tone. Laryngeal reflexes are maintained and active and attempted endotracheal intubation may precipitate laryngospasm. More responsive patients fight intubation by biting the tube off or spitting it out. However, respiratory depression may be delayed in appearance and necessitate a prolonged period of ventilatory assistance. Positioning and intermittent suctioning will preclude respiratory distress secondary to secretions in the posterior pharnyx.

Urine and blood samples should be collected at the time of admission and screened for phencyclidine, sedative hypnotics, ethyl alcohol, opiates and amphetamines. Urine samples should be capped to prevent loss of phencyclidine, which is volatile.

The Recovery Phase

Most acutely confused patients are communicative within 1-2 hours and alert and oriented within 6 to 8 hours of admission after ingesting the usual street dose. After they are alert and oriented, patients should be monitored for a minimum of two hours. Patients who remain oriented and alert and exhibit normal behavior can then be discharged.

If a patient remains stuporous or comatose, responding only to deep pain for greater than two hours, a minimal observation period of 24 hours is indicated. The recovery phase may vary from several hours to days depending on the route and the dose ingested.

Suicide has been reported during the "come down" period, 6 to 24 hours after taking phencyclidine. Patients should be informed about depression, irritability, feelings of isolation and nervousness that often accompany this period, and may last up to 48 hours.

All patients in whom coma is followed by a prolonged period of confusion should have a psychiatric evaluation prior to discharge. Persistent paranoia or depression may require transfer to a psychiatric unit.

Treatment

No agent is known to be specific for antagonizing the toxic effects of phencyclidine. However, some experience has been gained in the symptomatic treatment of seizures, hypertensive crisis, and aggressive and violent behavior.

Intravenous diazepam (Valium) in doses of 10 - 15 mg followed by intravenous diphenylhydantoin (Dilantin) has been effective in the control of seizures. In some cases it has been necessary to give an acutely confused patient 10 - 20 mg. of Valium orally to prevent injury to both the patient and staff. During the confusional phase of the prolonged recovery period, some patients have received repeated doses of 10- 15 mg of Valium to control motor restlessness and agitation. These therapeutic doses of sedative hypnotic agents do not appear to produce significant respiratory depression in phencyclidine intoxication.

Diazoxide (Hyperstat) has been used to reduce blood pressure during a hypertensive crisis associated with acute phencyclidine intoxication. Hydralazine hydrohloride (Apresoline) has also been suggested as a possible substitute agent.

Phenothiazines are contraindicated in acute phencyclidine intoxication where a confusional state is associated with hypertension, tachycardia ataxia and nystagmus. It has not been demonstrated that phenothiazines shorten the recovery phase or antagonize the behavioral effects of phencyclidine. In some cases they have produced prolonged, severe hypotension.

SUMMARY

Phencyclidine use appears to be in a growth phase nationally. Factors contributing to the increasing popularity include the user's ability to control the dosage, an understanding of the immediate effects, and its availability. Those most at risk appear to be young Caucasian males.

Phencyclidine-related problems are often like tips of icebergs, the underlying causes of which are hidden from public view. The problens often surface in the form of speech difficulties, memory loss, thinking disorders, personality changes, paranoia, severe depression, violence, accidents, suicides and homicides. Of particular concern to law enforcement personnel is the upsurge in phencyclidine-related violent crimes and carrying of weapons by users to protect themselves from their imagined persecutors.

The evidence currently available supports the assumption that if there is a solution to the problem of phencyclidine abuse, that solution is prevention. Therefore, medical personnel and others within the helping professions must be alerted to the fact that phencyclidine is not just another drug problem. The findings from users we have already studied strongly suggest that phenyclidine is not an "upper" or a downer,"I but perhaps an "insideouter," with long term implications.

FOOTNOTE

[1]The SES measure employed in this analysis was based on a formula which was especially developed for this analysis, and which was found to be more discriminating than the Hollingshead-Redlich formula. It included educational level of both parents, rather than only that of the head of the household, and also included codnsideration of the subject's income, and whether or not the family was on welfare, in addition to the occupational level of the head of household.

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Chapter 6

Phencyclidine and Ketamine Intoxication: A Study of Four Populations of Recreational Users

Ronald K. Siegel, Ph.D.

The time is 1926. In his laboratories at the University of Chicago psychologist Heinrich Kluver is just beginning the first experimental studies of the hallucinogen mesacaline. Derived from the peyote cactus which had been used by indigenous Indians throughout the New World for thousands of years, mescaline had only recently been isolated and synthesized, and was rapidly capturing the attention of researchers in Germany. But before this "classic" hallucinogen was fully investigated, other newer ones were being developed. Elsewhere in Germany, Kotz and Merkel (1926) had just reported the chemical groundwork for the preparation of a new compound, phencyclidine.

The time is 1959. Chen and his colleagues at the Research Laboratories of Parke, Davis and Company in Detroit have just "discovered" phencyclidine and observed its anesthetic effectiveness in animals. That announcement added one more drug to the rapidly growing list of psychoactive compounds, both natural and synthetic, which affect behavior. Yet science was just beginning to dwelop techniques for studying the effects of drugs on behavior. That year witnessed the publication of a new journal, Psychopharmacologia, officially announcing the pursuit.

It is now 1978. With such an evolutionary, albeit natural, lag between the emergence of a new drug and its scientific investigation, it is not surprising that today, a generation after phencyclidine's discovery, those people born when the drug was first developed are using and exploring its psychoactive properties while scientific investigations still lag behind. Nonetheless, reports fromuserswho first experiment with and experience the drug effects (the street drug users) provide a rational basis for the questions which researchers must ultimately attempt to ask and answer. Kluver's original studies of mescaline were based upon and guided by reports from people using the drug at that time. Similarly, present day studies of phencyclidine and its derivatives may be helped by examination of the patterns of use and intoxicationin contemporary nonmedical users. It is in this spirit that the following studies with phencyclidine and its derivative ketamine were conducted.

Phencyclidine and ketamine are chemical compounds known as arylcyclohexylamines. While many psychoactive drugs can be easily classified as either stimulants, depressants, or hallucinogens, the arylcyclohexylamines defy convenient classifications as they appear to have mixed excitatory, sedative, cataleptoid-anesthetic, and hallucinatory properties. The major questions concerning the use of these compounds by man are: (1) Why do humans initiate use of arylcyclohexylamines? (2) Why is such use maintained? and (3) What are the consequences of such continued use? These questions are addressed in this chapter. It will be presently seen that the psychological intoxication resulting from arylcyclohexylamines is a primary reason for their continued use. The nature and extent of thisintoxicationin several groups of contemporary users Will also be explored. Furthermore, it will be shown that the phenomenology of intoxication with these compounds warrants their classification as true hallucinogens.

I. PHENCYCLIDINE

STREET DISCOVERY AND INITIAL USE

Phencyclidine (PCP) or 1-(1-phenylcyclohexyl) piperidine hydrochloride was first reported in the context of nonmedical street use in the Haight-Ashbury district of San Francisco in 1967. At that time the drug was marketed as the PeaCe Pill or PCP (an abbreviation of the complete chemical name). While the Haight-Ashbury Free Medical Clinic reported that "use of the drug.... virtually ceased" by early 1968, it has remained consistently available under a wide variety of names. Such names include Hog, Angel Dust, Dust, Crystal, Crystal Joints, CJ, KJ, Peace, Peace Weed, Supergrass, Superweed, Rocket Fuel, Elephant Tranquilizer, Horse Tranks, Sheets, Seams, Surfer, Snorts, Scuffle, Cadillac, Cyclones, Sana, Mist, and Goon (cf. Perry 1975). Other more recent common names include Amoeba, Angel Hair, DOA (dead on arrival), Killer Weed, and Synthetic Marihuana (Young et al. 1977). This author has also doctumented the terms Lovely, Lovely High, and Super Kools. PCP is also the most prevalent drug in misrepresented street drugs (Perry 1977) and has recently appeared under the names THC, psilocybin, mescaline, and other hallucinogens Which are rarely available in pure form on the illicit market.

Cases of adverse reactions, unpleasant subjective experiences, poisoning, and prolonged psychoses are well known (e.g., Liden, Lovejoy, and Costello 1975; Rainey and Crowder 1975) and have probably attenuated some street use since 1971. However, the low costof PCP and its ease of production have contributed to its reappearance on the street (Burns and Lerner 1976). Indeed, one gram of PCP can make more than 24 "street joints" and doses as low as 3 mg are behaviorally effective. PCP's subjective effects include distortions in body image, hallucinations and dissociation. There can also be a preoccupation with death or death-related thoughts (meditatio mortis) and this has been the basis for numerous criminal defenses of diminished capacity (see "Phencyclidine, Criminal Behavior, and the Defense of Diminished Capacity," this volume). The prolonged and fluctuating effects are believed to be due to PCP's affinity for adipose tissue, its slow release from such tissue, and its subsequent selective uptake by brain tissue (Bums and Lerner 1976). Some adverse reactions are believed to be caused by related compounds TCP (1-(1-2-thienylcyclohexyl) piperidine) , and PCC (1-piperidinocyclohexanecarbonitrile), often produced in illicit syntheses. Related compounds such as PHP, which is 1-(1-phenylcyclohexyl) pyrrolidine, may also contribute to adverse reactions.

Nonetheless, users initially experiment with the drug primarily out of a curiosity about it and a desire to experience the anticipated drug effects of tranquilization, dissociation, and hallucinations. More often than not, initial use of PCP comes about as a result of users self-administering what they believe to be THC, psilocybin, or some other alleged drug. In these latter instances, PCP is often combined with LSD.

MAINTENANCE OF USE

The street users' initial encounters with PCP would have brought them into contact with both the unpleasant and pleasant effects of the drug. Independent of adverse reactions and even "schizophrenomimetic" or "psychotomimetic" effects, many users found the drug to have highly reinforcing properties. Indeed, the preclinical animal literature is rich with examples of PCP's powerfully psychoactive and reinforcing effects (Balster and Chait 1976), and PCP represents one of the only hallucinogens that monkeys will reliably self-administer. While it is difficult to determine the unique properties that reward such animal behavior, the euphoria, inebriation, and hallucinatory effects are undoubtedly responsible for maintaining PCP use in man. The effects can be interpreted as a state of intoxication with high reinforcement potential. While many nonpharmacological factors (e.g., easy and inexpensive illicit synthesis) may affect man's use of a drug such as PCP, psychological intoxication appears to be the primary reinforcing effect.

These PCP intoxications can vary greatly among users. Pollard, Uhr, and Stern (1965) examined the effects of 10 mg (p.o.) in a modified sensory deprivation situation. One of their college student subjects described a typical experience marked by a preoccupation with abnormal bodily sensations, lack of visual imagery, and marked feelings of depersonalization:

> I feel like I can't think anything even. And I can't express myself even if I can think because it's hard for me to talk. My lips are numb. It's so uncomfortable. My perception is very bad. Nothing is clear . . . . My mind is just a complete blank....I have such a strange feeling. I can't explain it. Like I'm still asleep, yet I'm not asleep. I'm awake (pp. 89-90).

Other subjects in this study described these sensations as "I feel dissociated with the world" (p. 131) and "I feel dead" (p. 134). Luby and co-workers (1959) administered 1 mg/kg, i.v., to normal subjects who reported body image changes, estrangement, disorganization of thought, negativism and hostility, drowsiness and apathy, hypnagogic states, feelings of inebriation, and repetitive motor behavior.

These authors described the hypnagogic states as resembling pseudohallucinations wherein subjects "reported feeling as though they were in some specific setting and were able to describe it in detail. While the reports typically had reference to past events, they were expressed as though the experiences were taking place at the moment. The lack of time-boundedness was reminiscent of dreaming. As in dreams, multiple shifts occurred in the settings experienced by the subjects, sometimes in rapid succession" (p. 366). Sometimes the subjects reported euphoria and feelings of inebriation: "When it occurred, the subjects would often smile vacuously and compare their feelings to those resulting from several Martinis" (p. 366).

Most users have difficulty in describing this intoxication and simply report a state of oblivion and fantasy. Perry (1975) summarizes some of the psychological effects of this state:

> The high continues for 4-6 hours, during which time the user often becomes very talkative, having sincere and sympathetic conversations, usually with others similarly intoxicated. This gradually develops into a state of mild depression as the high wears off; the person is irritable, feels isolated and sometimes paranoid. These users generally require 24-48 hours to completely return to what they consider normal (p.2).

Many users find the experience a positive one and emphasize the rewarding aspects of the same symptoms that other users cite as negative. Consider the following account provided by one of the author's respondents:

> Immediately after smoking the Dust (PCP) I started experiencing the effects. All my troubles seemed to go away. I felt a little drunk and had some trouble walking around the apartment. Objects appeared either very far away or very close and I couldn't really judge distance at all. This reminded me a lot of Acid (LSD). I closed my eyes for a while but didn't see much more than a few colored geometric patterns. Not nearly as trippy as other psychedelics, but it was clearly a psychedelic. I liked being apart from things, and felt outside my body for most of the trip. That was fun. Before I smoked I had been troubled about some exams coming up and felt I wasn't really prepared. All that anxiety vanished with the

> Dust. I even looked at my books and work but couldn't get excited about it. I felt at peace. It was a good feeling. When I started coming down, I felt sad that I was leaving such a lovely place. I think I even cried. I hadn't done that in years. But most of all, I remember the peace and tranquility. Everything was good. I want to be there always. That's why I like to call Dust PPP - Perpetual Peaceful Place.

Recent studies of phencyclidine users are beginning to uncover an increased occurrence of these pleasurable and positive effects among those who continually self-administer the drug. For example, Walters (1978) has studied a group of multiple drug users in Philadelphia, primarily intranasal PCP users, and found that PCP use is rarely involved with PCP-related emergencies or clinical crises:

> Our respondent population is small, somewhat transient and currently just under 50 youths ranging in age from 14 to 24 years, divided about evenly between males and females. Of these, 34 have some history of PCP use, with 15 of them using it between five and 10 times per week. Finally their histories of PCP use range from between one and seven years, with three years' use being average. Yet by far, most of the drug-using youths with whom we have had contact are not dulled, depressive, anomic bundles of pathology described in the literature and the media. Rather, they are bright, level-headed and stable and eager and willing to experience life, including drugs that are a part of that life (p. 9).

Stickgold (1977) has recently commented on the emergence of PCP as a drug of choice among may users. He describes this population of users:

> Those who are today using PCP, tend to come from a different place, both socio-economically and in their drug-taking behavior. Rather than the middle class seekers of the new sensate worlds to explore, PCP is, today, becoming the drug of choice of the lower class oppressed minority group member seeking an escape from persecution. In the past s/he has found this escape in other depressant drugs such as heroin and barbiturates. Today PCP not only provides that escape, but also produces a degree of increased awareness that is different enough to be interesting, and mild enough not to be too frightening (p. 2).

CONSEQUENCES OF CONTINUED USE

Despite the obvious negative effects, and the apparent attractiveness of the positive effects, the consequences of continued phencyclidine use are still largely unknown. The rather prolonged recovery time from acute intoxication, sometimes lasting as long as 15 days (Burns and Lerner 1976), confuses the issue of long-term effects. In addition, the persistent psychoses seen in a very small number of cases (Burns and Lerner 1976; Fauman et al. 1976) may represent either a psychopharmacological effect from the drug or an individual sensitivity to it. Nonetheless, most investigators agree that these psychiatric sequelae of continued phencyclidine use can be serious and represent classic schizophrenic symptoms. With still other chronic users, there is both preclinical (e.g., Balster and Chait 1976) and clinical (e.g., Burns and Lerner 1976) evidence to suggest tolerance to the psychological effects of phencyclidine requiring use of increasing doses. Psychological dependence, albeit not physical addiction, appears prominent among long-term users.

Recently, Ashley (1978) has commented on the consequences of continued use among PCP users or "peepheads":

> Chronics users clearly enjoy PCP and experience it in a positive way. . ..Most say it takes a few days to return to normal, but many of them don't bother to and use the drug every day.... (they) almost always complain of being spaced and worry about turning into 'vegetables'. They are noticeably depressed when not high, so much so that some have committed suicide at this point. Serious accidents are commonplace among users. Almost all report having been in an automobile accident or knowing someone who was, while on PCP. Falls are common, even off cliffs or out of boats and windows. Impairment of motor and sensory functions makes many normal physical activities dangerous (p. 64).

VARIABLES AFFECTING USE AND INTOXICATION

The precise description of the state of phencyclidine intoxication requires information about concomitant variations between the characteristics of the behavior and the drug (cf. Siegel 1977a). Information about the behaviors should be specific with-respect to individual variability, type of behavior and behavioral history. Information about the drug should be specific with respect to dose, adulterants, routes of administration, dose-response and time-response relationships, among others. Such variables can be further modified by environmental variables such as set and setting. While a full understanding of these interactions is presently restricted by limited knowledge concerning arylcyclohexylamines, the presence of such a myriad of interacting variables should temper a desire to simplify use and intoxication with succinct labels such as "lovely high," "perpetual peaceful place," "psychotic," or "schizophrenomimetic." The studies described below were undertaken in an attempt to elucidate some of these variables in relation to the psychological intoxication.

THE SAMPLE

A large population of recreational drug users, recruited through advertisements in several Los Angeles area newspapers, was initially screened. by a telephone interview and a subsequent drug history questionnaire. A total of 319 phencyclidine users (referred to as Adult Group) were eventually selected for study. All subjects in the sample met the initial requirement of having used PCP more than once in the last year. All subjects were male, 21-38 years old, and were examined and tested in the Neuropsychiatric Institute at UCLA. Examination procedures included a personal history questionnaire, drug history questionnaire, mental status examination, Minnesota Multiphasic Personality Inventory (MMPI), Experiential World Inventory (El-Meligi and Osmond 1970), in-depth interview, physical examination (for most subjects) and visual imagery and perception tests.

One additional group of chronic PCP subjects was also recruited for study. This latter group (referred to as Juvenile Group) consisted of 20 juvenile males, 14-17 years of age, who were initially referred to the author for evaluation by the courts or law enforcement officials. All subjects in this sample met the initial requirement of having used PCP at least once per week for the previous 6 months.

MULTIPLE DRUG USE

All subjects in the Adult Group had past or present histories of multiple drug use. Concomitant with their use of PCP, 86 percent were using caffeine preparations; 81 percent were using alcohol; 81 percent were using cannabis preparations: 62 percent were using hallucinogens other than cannabis; 58 percent were using tobacco products; and 20 percent were using cocaine, amphetamine and other stimulants. Prior to their PCP use, subjects reported experiences with barbiturates (11 percent), tranquilizers (10 percent), and opiates (2 percent).

All subjects in the Juvenile Group had past or present histories of multiple drug use. Concomitant with their use of PCP, 100 percent were using caffeine preparations (mostly cola beverages and chocolate); 40 percent were using alcohol: 40 percent were using cannabis preparations: and 15 percent were using barbiturates. Prior to their PCP use, some subjects (20 percent) reported experiences with stimulants while one (5 percent) used heroin intranasally. Interestingly, none of the Juveniles had tried hallucinogens other than cannabis, while 16 (80 percent) had used volatile solvents in the past.

PREPARATIONS AND PURITY

All subjects used PCP in the form of either tablets, capsules, powders, botanical mixtures, or liquids. It should be noted that Helisten (1977) has reported that 88 percent of street THC samples contain either PCP, PCP and PCC, or PCP and other drugs. Almost

5 percent of street THC samples are combinations of TCP and PCC. Since these are all arylcyclohexylamines, whenever subjects in these studies reported use of street THC, it was recorded as PCP use. Lundberg, Gupta, and Montgomery (1976) have identified the quantitative and qualitative aspects of street PCP in the Los Angeles area. They report that tablets contained 1.0-6.4 mg each (mean of 5.3 mg); powder averaged 88-100 percent PCP; botanical leaves (usually mint or parsley leaves) varied from 0.2-7.9 percent; and prerolled cigarettes ranged from 1.0-3.0 mg total for each cigarette. Another street drug assay laboratory in California (PharmChem, Palo Alto) has found some parsley "joints" of PCP containing from 3.2-28.3 mg of PCP (Perry 1975). The most common adulterants for samples received by these laboratories are LSD and TCP. Recently, NIDA (DuPont 1977) has noted that street preparations of PCP may be combined with other psychoactive drugs including heroin, cocaine, methaqualone, methylenedioxamphetamine (MDA), aspirin, and caffeine. Liquid forms of PCP are usually diverted licit vials of Sernylan (formerly called Sernyl, phencyclidine hydrochloride, from Bio-Ceutics Laboratories in Missouri). These vials are usually 10 ml each with each ml containing either 20 or 100 mg. Illicit PCP in liquid form is often seen in small "cokevials" or similar glass bottles.

The most common street preparation is in the form of botanical mixtures sometimes referred to as leaf mixtures. These consist of PCP mixed with mint leaves, oregano, or parsley. Rarely catnip is used and, because of the hallucinogenic nepetalactone oils present in this material, the resultant mixture may be more hallucinogenic than PCP alone. Lundberg, Gupta, and Montgomery (1976) also report that marihuana or other cannabis products are sometimes present in street PCP material.

The Juvenile Group often employed a special preparation called "Super Cools." This consisted of a mentholated tobacco cigarette that had been dipped in liquid PCP and dried. The additive effects of nicotine and PCP in such preparations often resulted in states of extreme intoxication.

ROUTES OF ADMINISTRATION

In the Adult Group, 280 subjects (88 percent) had experience with smoking PCP preparations, 38 subjects (12 percent) had orally ingested tablets or capsules, 15 subjects (5 percent) had used PCP intranasally via snuffing or snorting, and three subjects (0.9 percent) had injected PCP intramuscularly.

All 20 Juvenile subjects (100 percent) used PCP exclusively via the smoking route.

DOSAGES

A number of researchers have attempted to calculate dosages employed in recreational use of PCP. Burns and Lerner (1976) have estimated that the average amount smoked "per episode" is 35-75 mg, usually delivered in one or two cigarettes or "joints." When PCP was used intranasally, subjects usually self-administered one "cokespoonful" per nostril or one "line" per nostril. The amount of pure PCP in commercially available "cokespoons" has been determined (by this author) to range from 3.5-7.1 mg for a level cokespoon. Assuming an average street purity of 95 percent (cf. Burns and Lerner 1976), this amounts to an average intranasal dose of approximately 10 mg (total for both nostrils) per administration. The average line of PCP is about 0.5 x .15 inches and amounts to approximately 5 mg of PCP if pure or 4.75 mg if street PCP is used. Since two lines are used per administration, this amounts to approximately 9.5 mg, considerably more than previously estimated (cf. Burns and Lerner 1976). when PCP is taken by mouth, the average dosage is estimated to be 5 mg.

DOSE REGIMES

Subjects in both the Adult and Juvenile Groups fell into several patterns of PCP use (discussed below). In general, when smoking the drug, Adult subjects tended to "titrate" or adjust their dose intake to what was perceived to be an optimal level of intoxication. Most subjects (Adults) used approximately one cigarette per week in this manner (range = 0.3-4.0). This amount was generally consumed in one episode per week. When Adults used PCP intranasally or orally, a single administration would occur approximately once every 8 weeks. In the Juvenile Group, 10 subjects (50 percent) reported that they always attempted to titrate their use but these users consumed approximately 28 grams of leaf mixture per month each. However, doses were not evenly distributed across time. Generally, Juveniles consumed their supply within a few days, but such use was marked by much sharing and selling among peers. The remaining 10 Juvenile subjects reported that they always attempted to stay chronically intoxicated and used approximately 5 cigarettes per day (range = 2-20).

These doses and dose regimes have created what researchers have generally agreed are three distinct levels of intoxication: low (5-10 mg), moderate (10-20 mg), and high (100 + mg). (See Burns, Lerner, and Corrado 1975 for discussion of dose-effect relationships).

PATTERNS OF USE

The dose regimes together with the set and setting define the pattern of drug use. Five patterns of drug use have been designated by The National Commission on Marihuana and Drug Abuse (1973) and will be used for discussion here.

Experimental Use

Of the 319 Adult subjects, 267 (84 percent) were classified as experimental users engaged in short term, nonpatterned trials of PCP with varying intensity and a maximum frequency of 10 times in their entire drug history. These users were primarily motivated by curiousity about PCP and a desire to experience the anticipated drug effects of tranquilization, euphoria, inebriation, dissociation, and hallucinations. Their use was generally social and among close friends. Most did not enjoy the experience and did not express a desire to repeat the drug use. Interestingly, most of the Adult users endorsed the street myth that PCP is a "bad" drug that inevitably produces adverse reactions. Only those experimental users who expressed a belief that their PCP was really THC or some other drug also expressed a desire to continue using it beyond the experimental stage. These latter users typically claimed that PCP was simply "strong marihuana and something you could probably learn to handle." This latter finding suggests the importance of psychological set and setting in determining drug reactions.

None of the Juveniles were classified as expertimental users.

Social-Recreational Use

The remaining subjects in the Adult Group (52, or 16 percent) were classified as social-recreational users who engaged in more regular use than experimenters. Use generally occurred in social settings among friends or acquaintances who wished to share an experience perceived by them as acceptable and pleasurable. These users were primarily motivated by social factors and their use was always voluntary. It did not tend to escalate to more individually oriented patterns of uncontrollable use. Many of these Adult subjects started as expermental users but only 12 of them (23 percent) engaged in episodes of more frequent use (see below), although their primary pattern was the social-recreational one.

In the Juvenile Group, 10 subjects (50 percent) were classified as social-recreational users. Unlike their Adult counterparts, these Juveniles all tended to engage in more frequent patterns of use.

When asked to rank all drugs in terms of recreational drugs of choice, the Adult social-recreational users ranked cocaine first, cannabis second, and, surprisingly, PCP third. This may be related to the findings that both PCP and cocaine share similar sympathomimetic effects (Chen, Ensor, and Bohner 1965). When asked to rank all drugs in terms of potency in producing intoxication, 93 percent ranked PCP first. Other drugs ranked above PCP in this category included LSD and Ketamine (discussed in the second part of this chapter). Juveniles ranked marihuana first as a recreational drug of choice and PCP second. All Juveniles also ranked PCP first in potency.

PCP retained popularity as a recreational drug among may Adults and Juveniles for several reasons:

1) PCP was viewed by Adult users as a misunderstood drug which opened new altered states of consciousness for exploration. These states were considered to be unobtainable

or less easily reached via conventional hallucinogens.

2) PCP was viewed by Juvenile users as economical and readily available.

3) PCP was viewed by both Adults and Juveniles as an extremely effective and different hallucinogen that could induce intoxication quickly and with such rapid onset of action allow one to titrate dose. It was considered by these users to be a "social hallucinogen" which, because of the paucity of visual effects, allowed the user to be more social than with the more "visual" psychedelic hallucinogens like LSD.

most social-recreational users felt that the possibility of unpleasant and adverse reactions was a rate-limiting determinant of PCP use. Consequently, they engaged in stable, low frequency patterns of use which did not escalate to individually oriented patterns of uncontrollable use. They also felt that PCP was not physiologically harmful but rather "expanded consciousness" in long-lasting ways. Indeed, many of the Adults felt that the drug took the user "to places that LSD only suggested were there" and "with PCP the afterglow stays with you for a long time."

Circumstantial-Situational Use

Only three Adult users and four Juveniles engaged periodically in circumstantial-situational use, defined as a task-specific, self-limited use which was variably patterned, differing in frequency, intensity, and duration. This use was motivated by a perceived need or desire to cope with a specific condition or situation. The motivations cited by users, in order of decreasing frequency, were: to alleviate the dysphoria associated with situation depression (81 percent); to enhance appreciation of social situations or musical events (73 percent); and as general entertainment when other recreations were unavailable (56 percent).

Intensified Drug Use

Nine Adult users (3 percent) and 10 Juvenile users (50 percent) engaged in episodes of intensified use characterized by long term patterned use of at least once a day. Such use was motivated chiefly by a perceived need to achieve relief from a persistent problem or stressful situation, or a desire to maintain a certain self-prescribed level of intoxication. Nonetheless, users here referred to their intensified use as "too much," "loaded most of the time," "really Dusted," or "bombed." or "toasted" and were aware of negative effects including unpleasant feelings. For most intensified users this subsequently curtailed such patterns of intensified use for varying periods of time.

Compulsive Drug Use

None of the subjects studied engaged in compulsive use, which is characterized by high frequency and high intensity levels of relatively long duration, producing some degree of psychological dependence. Two Adult users did appear to become compulsive users, but they dropped out of the study before adequate assessments of their behavior could be made.

PHENOMENOLOGY AND INCIDENCE OF INTOXICATION EFFECTS

The acute physiological and psychological effects reported by users did not differ substantially from these described in the literature (e.g., Burns and Lerner 1976) or elsewhere in this volume. Briefly, subjects (Adults and Juveniles are combined here) repeatedly sought and experienced heightened sensitivity to stimuli (94 percent), stimulation (92 percent), dissociation (88 percent), mood elevation (61 percent), inebriation (55 percent), relaxation or tranquilization (53 percent), hallucinations (30 percent), increased sociability (14 percent), increased cognitive activity (11 percent), and euphoria (8 percent). A number of untoward effects were also reported by the users: perceptual disturbances (78 percent), restlessness (76 percent), disorientation (63 percent), anxiety (61 percent), paranoia (34 percent), hyperexcitability (27 percent), irritability (22 percent), mental confusion (22 percent), and partial amnesia (18 percent). Dysarthria was not assessed in the questionnaire but roughly 80 percent of the respondents in the interviews admitted having experienced this effect as well.

Taken together, individuals reported experiencing negative or untoward effects in all intoxications and positive or desired effects in only 60 percent of the intoxications.

The chronic effects reported by the Intensified Drug Users were also similar to those reported elsewhere in the literature. In addition to acute intoxication phenomena, users experienced both desired and undesired effects. The desired effects included: a generalized feeling of well-being and detachment from worldly tensions and anxieties (65 percent), heightened perceptual sensitivity in some modalities (43 percent), and psychedelic or transcendental reactions (8 percent). The undesired effects included: disturbances in time perception (38 percent), nervousness and irritability (38 percent), perceptual disturbances (31 percent), fatigue or lassitude (27 percent), and memory disturbances (25 percent).

Overall, chronic negative effects experienced in all intoxications, while positive effects were experienced inapproximately 74 percent of the intoxications.

HALLUCINATIONS AND PSYCHOSES

Of the phenomena reported above, the changes in perception,mood, and thinking are perhaps the least understood but also among the most important in determining the precise nature and form of PCP intoxication. Indeed, Domino and Luby (1972) have suggested that these abnormal states induced by PCP strongly resemble schizophrenia, especially in creating profound perceptual and cognitive disorganization and occasionally catatonic immobility. Furthermore, the presence of perceptual changes such as hallucinations is a key diagnostic criterion in the determination of the psychotic phase. Therefore, these perceptual changes were the subject of concentrated examination and testing in the study.

The definition of the word hallucination (which comes from the Latin Hallucinari, meaning to prate, to dream, or to wander in mind) is far from precise. However, a widely accepted definition in psychiatry is: "A false sensory perception in the absence of an actual external stimulus. May be induced by emotional and other factors such as drugs, alcohol and stress. May occur in any of the senses." By this definition, it is not surprising that most PCP users have experienced hallucinations. For most such subjects (94 percent) these consist of a wandering in mind or attention which is manifested as lapses in attention, mental confusion, clouding, and related phenomena. Such experiences include difficulty in maintaining attention during complicated tasks: difficulty in maintaining thoughts during conversation; and general preoccupation with subjective sensations. These effects are similar to those Domino and Ludy (1972) have described as "attention disorder," "withdrawal," and "clouding delirium."

The most common perceptual disturbance was a change in body image. Luby and co-workers (1959) have described this state as "accompanied by loss of 'ego boundaries', impaired ability to distinguish self and nonself stimuli, feeling of depersonalization, and a sense of unreality" (p. 364). Generally, subjects reported that their bodies felt strange and distorted and these feelings were usually coupled with changes in tactile sensations. Visual changes included macropsia and micropsia, while tactile changes included numbness and paresthesias.

The most common mood disturbance was a blanding of affect, although many users tended to admit that this made them somewhat euphoric in light of pre-existing dysphoria. Previous researchers have described this as "ambivalence" and "affect disorder." Undoubtedly, these changes in mood contributed to the feelings of dissociation or estrangement from self and body which were commonly reported.

The most common thinking disturbances have been described in the literature as "loosening of association," "overinclusive thoughts," "concreteness," "delusional thinking," and general "disorganization" Associated with these phenomena are "negativism" and "hostility." In order to assess these states, the MMPI and the Experiential World Inventory (EMI) were administered. Only the intensified Adult and Juvenile users manifested abnormal profiles on these tests. The most consistent high point on the EMI was the ideation scale, which strongly suggests thought disorder including unbridled fantasy activity, inability to connect experiences purposefully, flights of ideas, and serious loss in the capacity to select and resist thoughts and to produce and connect new thoughts. Other consistently high scores were seen on both sensory perception, time perception, and body perception scales. Surprisingly, the impulse regulation scale, an indicator of hostility and violence, was usually the lowest point on the profile. The MMPI profile for these intensified users indicated a large number of experiences and symptoms which are characteristic of psychotic thinking, including hallucinations, delusions, paranoia, feelings of unreality, and a general sense that things are wrong. The MMPI content scales also indicated a large number of symptoms of the type sometimes associated with organic involvement of the central nervous system. Complaints here included skin sensations, nausea, dizziness, and difficulty with speech, memory, concentration, ability, coordination and motor control. Unlike the EWI results, the MMPI profile indicated that most of these users were distractable and when faced with frustration might become irritable, aggressive, or impulsive, often out of proportion to the reality of the situation. Taken together, these findings indicate that PCP produces many of the symptoms characteristic of schizophrenia, although it most be emphasized that the correlation of symptoms does not imply a direct causal relationship.

II. KETAMINE

In the 1959 horror film, The Tingler, actor Vincent Price injected himself with the little-known drug LSD in order to produce a state of fear and panic. That single cultural incident heralded a much wider phenomenon of LSD use during the psychedelic revolution of the Sixties. In the 1976 film, Family Plot, Alfred Hitchcock depicted a kidnap victim sedated with a little-known drug called ketamine. Once again the cultural productions of man acted as a barometer of the social times, as the Seventies are witnessing a growing problem of ketamine abuse.

DISCOVERY AND INITIAL USE

Dissatisfied with the clinical experience of PCP as a surgical anesthetic druq (the duration of action and emergence excitement were too great to recommend use of the drug), Parke Davis and Company developed a congener of PCP for anesthesia in man. The drug was called ketamine hydrochloride or 2-orthochlorophenyl, 2-menthylamino cyclohexanone hydrochloride (original code name CI-581). Marketed under the names Ketalar (Parke Davis and Company), Ketaject (Bristol Laboratories and Ketavet (for veterinary purposes), ketamine is rapidly emerging recreational street drug.

Ketamine was enthusiastically described as a nonbarbiturate anesthetic that is a "rapid-acting general anesthetic producing an anesthetic state characterized by profound analgesia, normal pharyngeal-laryngeal reflexes, normal or slightly enhanced skeletal muscle tone, cardiovascular and respiratory stimulation, and occasionally a transient and minimal respiratory depression" (Bristol official package circular for Ketaject). Anesthesiologists endorsed its use initially because surgical patients remained physiologically very strong and required little support of vital processes. Surgeons were also impressed with the rapid action but somewhat disturbed when patients appeared responsive to stimuli in the operating room. Gradually the clinical experience demonstrated that ketamine produced a number of complications from which it was originally claimed to be free. The complications included: "severe laryngospasm and respiratory arrest in neonates, cardiac arrest secondary to respiratory depression in an adult, severe airway obstruction with vaniting and aspiration in children, and hysterical postanesthetic reaction" (Clin-Alert 1971). Indeed, these latter emergence reactions have been variously described as "confusional states," "vivid dreaming," "hallucinations," and "preseizure and seizure activity."

Nonetheless, the drug produced extremely effective analgesia which was still judged useful in certain situations such as for burn dressings and radiotherapy, in emergency field work, and in war conditions. Indeed, the drug enjoyed popularity among surgeons as the most widely used battlefield anesthetic in Vietnam. The analgesia is probably achieved through the drug's dissociative action in that it appears to selectively interrupt association pathways of the brain before producing somesthetic sensory blockade (Sparks et al. 1973; Weingarten 1972; Winters 1975). Some observers (e.g., Young et al. 1977) attribute the present popularityof the drug to experiences gained among patients in Vietnam and elsewhere during the late 1960's.

Street use of ketamine hydrochloride solutions was first noted in 1971 in San Francisco and Los Angeles (Siegel, personal observation), while other forms of ketamine (e.g., powders, tablets, etc.) were first noticed on the street in 1974 (Ashley 1978). Solutions go under a variety of street names including: Ketalar, Ketaject, Ketavet, K, Kay, Jet, Super Acid, 1980 Acid. Powder forms of ketamine on the street as: Green, Purple, Mauve, Special LA Coke, Super C, and K. For both medical and nonmedical users, the emergence reaction characterized as adissociative hallucinatory period is probably the most dramatic aspect of the ketamine experiencee.

MAINTENANCE OF USE

The ketamine dissociative reactions, while producing analgesia, also produce classic hallucinogenic reactions which undoubtedly motivate recreational users. These reactions were originally described in the anesthesiology literature (e.g., Kreuscher 1969) as emergence reactions that could be quickly "managed" or suppressed via treatment with a variety of agents such as diazepam, droperidol, fentanyl, pentobarbital, or meperidine (e.g., Wantz 1977). Doenicke and co-workers (1969) reported on the phenomenology of this reaction when it was not suppressed by other medications. Both their patients and experimental subjects experienced analgesia concomitant with depersonalization, derealization, changes in body imagery, nausea, dizziness, dreams, and hallucinations. Most of their subjects stated that the dream period and hallucinatory phase was "pleasant" and a typical description of the intoxication follows:

> During the first subjective experience, I imagined myself in a complicated system of pipes which reminded me of an oil refinery. A driving force shot me through the colorful, occasionally angled, pips. I was wondering about the provenance of these strange circumstances and believed I had been hexed by relatives . Now this seemed to be my eternal fate, which made me very sad. Some time later, I was first able to perceive acoustic impressions from my surroundings, which previously had been missing. The voices of the people present in the room sounded distant, but yet loud and resounding. I could hear the sounds, but I could not understand them. I thought that they were voices of relatives who had hexed me. Later I was able to perceive visual impressions. The room appeared dusky-foggy to me. In the distant opening of a pipe appeared the head of a colleague. Now I understood a few words and began to answer. My speech sounded babbling and booming to me. Intermittently the hallucination of being hexed returned. Later I was told that I had uttered strange sounds. My tongue seemed to me to be extremely big, but very light. In my extremeties, too, I felt a striking lightness. Shortly before awakening, I was again able to understand what was said around me and I saw my surroundings again, though greatly blurred and constantly revolving around me (pp. 149-150, translated from the German by R.K. Siegel).

Rumpf and colleagues (1969) found their subjects described ketamine hallucinations as "utopic," "phantastic," "unreal," or "mysterious." Only one out of their 18 subjects considered the dream experiences normal and ordinary. The experience was termed pleasant by 6 subjects, unpleasant by 8, and neutral by 4. Experiences reported by these test subjects included dreams of recent memories, feelings of floating in space or falling or riding in various vehicles, vividly colored (primarily red) geometric patterns and designs, and were in general similar to the phenomenology of other drug-induced hallucinations (see Siegel 1977b). Unexpectedly, Rumpf and colleagues reported that fully one third of the experimental group (6 subjects) had true hallucinations with the concomitant delusions that their dreams were not dreams, but, in point of fact, real events! Such intense hallucinations are rare in drug-induced experiences (Siegel and Jarvik 1975).

In a well controlled study, Collier (1972) demonstrated that most ketamine dreams or hallucinations were judged by subjects as pleasant and of unusual intensity. One dream sequence was markedly transcendental as "the patient ascended to Heaven, saw God and was re-incarnated in Italy. Luminosity, green colour, tranquility and marked euphoria predominated. This these continued for over 2 hours into the awake phase during which he thought that he was speaking Italian. A central object blindness occurred. Six months later he had not experienced any similar dreaming or spontaneous phenomena but still remembered the episode vividly" (p. 125).

Current recreational users of ketamine appear to be motivated to achieve these dissociative hallucinatory states. Young et al. (1977) likens this state to an LSD trip, only the ketamine tripper "feels as if he is floating in a dreamlike state while experiencing vivid visual images" (p. 107). Stafford (1977) has recently cited a report from a current recreational ketamine user which illustrates the romantic appeal of the state similar to the "perpetual peaceful place" described by PCP users:

> And when I closed my eyes a lot of information started to happen. Colors, patterns, cross-connections in sensory perception. Like sound and inner visions sort of got confused. I got deeper and deeper into this state of realization, until at one point the world disappeared. I was no longer in my body. I didn't have a body. And I reached a point at which I knew I was going to die.... .And what incredible feelings that evoked! . . . . . .I just yielded. And then I entered a space in which . . .there aren't any words.....I mean, at-one-with-the-universe, recognizing-your-godhead.....The feeling was: I was home. That's really the feeling of it. And I didn't want to go anywhere, and I didn't need to go anywhere. It was a bliss state. Of a kind I had never experienced before. I hung out there awhile, and then I came back. I didn't want to come back. I guess in the deep state it was no longer than half an hour (pp. 348-349).

CONSEQUENCES OF CONTINUED USE

During the acute intoxication with ketamine, there is significant impairment in attention, learning, and memory functions (Harris et al. 1975). In particular, subjects have impairment in organizing and understanding the enviroment during emergence reactions. But few, if any researchers have documented the long term consequences of continued use of this drug. In preclinical animal studies, chronic ketamine administration results in abnormal brain wave activity, and withdrawal is marked by progressive increases in epileptiform activity without gross behavioral manifestations (Manchar, Maxwell and Winters 1972). Since such abnormal electrical activity in the brain is not correlated with observable changes in behavior, it is not surprising that clinical studies have failed to detect any long term impairment of behavior or personality functioning. Nonetheless, "bad trips" are frequent can result in paranoia and fear of subsequent similar intoxications (see Johnstone 1973).

A number of studies have documented recurrent hallucinations following ketamine anesthesia as well as flashbacks (Fine and Finestone

1973; Perel and Davidson 1976), and some have even suggested, albeit weakly, resulting psychoses (Johnson 1971). While the incidence of ketamine flashbacks far exceeds that for other hallucinogens (Siegel and. Jarvik 1975), the presence of flashbacks and allied perceptions does not normally present psychological problems; for the patients or users. Indeed, a number of psychiatric investigators have utilized continued treatment with ketamine to create abreactive effects in psychotherapy and research settings (e.g., Khorramzadeh and Lofty 1973; Lilly et al. unpublished).

VARIABLES AFFCTING USE AND INTOXICATION

The variables affecting intoxication with ketamine are similar to those discussed above with reference to phencyclidine. In addition, because of the more profound hallucinatory quality of the ketamine experience, intoxication is greatly influenced by set and setting. Because ketamine induces an extreme sensitivity to environmental stimuli, the physical surroundings are particularly important. Indeed, recovery personnel in hospital operating rooms have long since learned the importance of isolating the ketamine patient from intense light, noise, and other stimulation. The intrusion of even the most innocent stimuli such as monitoring the patient's vital signs can trigger hyperexcitability, psychomotor activity, and even seizures. Accordingly, recovery from ketamine anesthesia is usually handled with minimal verbal and tactile stimulation in medical settings, but rarely is this precaution observed in non-medical situations. Furthermore, since ketamine is often injected either intramuscularly or intravenously, such factors as sterile procedures and instruments, purity of the solution, and site of injection are especially important determinants of the intoxication. Respiratory depression may occur from overdosage and the presence of sedative drugs (barbiturates, opiate narcotics, etc.) in the body may also influence the intoxication and risk of overdosage.

THE SAMPLE

Two separate populations were sampled for studies of recreational ketamine use. One population (referred to as the Intranasal Group) consisted of recreational users recruited from a previous study of cocaine use (Siegel 1977a). Another population (referred to as the Injection Group) consisted of recreational hallucinogen users recruited from a previous study (Siegel and Jarvik 1975). A total of 10 Intranasal users and 13 Injection users were eventually selected for study. All subjects in the sample met the initial requirement for having used ketamine more than once in the last year. Subjects were approximately equally divided between men and women, 21-45 years of age, and were examined and tested in the manner described in the phencyclidine section of this chapter.

MULTIPLE DRUG USE

All subjects in the Intranasal Group had past or present histories of multiple drug use. Concomitant with their use of ketamine, 100 percent were classified as social-recreational users of cocaine (see Siegel 1977a). All subjects in the Injection Group also had past or present histories of multiple drug use. Their use of ketamine ran parallel to their use of other hallucinogens and fully 77 percent were currently using LSD. Interestingly, none of the Intranasal or Injection users were using phencyclidine, although two subjects from each group had experimented with it in the past.

PREPARATIONS AND PURITY

All subjects used ketamine hydrochloride in the form of capsules, powder, crystals, tablets, or solutions. Solutions are usually diverted legal vials of ketamine available in concentrations of 10 or 50 mg/ml (Ketaject) or 10, 50 or 100 mg/ml (Ketalar). An occasional street adulterant of these solutions is vitamin B_{12} due to a common street myth (partially true) that this attenuates adverse reactions. Capsules (usually clear, red, or black/yellow), powders (green, mauve, or white), crystals (white), or tablets (usually white) are usually mixtures of ketamine hydrochloride and various nonpsychoactive compounds such as lactose, flour, talc, and vitamins. The most common psychoactive adulterant found in powders or crystals is cocaine hydrochloride, although others including amphetamines and caffeine are also found. At the present time no quantitative information is available on these preparations.

ROUTES OF ADMINISTRATION

By definition, all subjects in the Intranasal Group employed the intranasal route of self-administration, and none of these users had ever experimented with other routes of ketamine administration. Similarly, all subjects in the Injection Group employed the intramuscular (i.m.) route of self-administration. However, of the 13 subjects here, four subjects experimented with intravenous (i.v.) injection and one subject had experimented with smoking ketamine.

DOSAGES

Little reliable information on recreational intranasal dosages of ketamine is available. Young and colleagues (1977) estimate that "the normal abuser's dose is 50 mg" (p. 107). However, judging from the reactions and intoxications reported by users (see below) it is estimated that intranasal doses range from 60-100 mg. For Injection users, the surgical anesthetic dosages range from 6.5 to 13.0 mg/kg (i.m.) and 1.0 to 4.5 mg/kg (i.v.). Recreational Injection users employ dosages of approximately 1.0 to 2.0 mg/kg (approximately 0.5 to 1.0 mg/lb.) for both intramuscular and intravenous administration.

DOSE REGIMES

Subjects in both the Intranasal and Injection Groups fell into several patterns of ketamine use (discussed below). In general, when using the drug intranasally, subjects tended to administer the drug only once in any given episode and to repeat episodes of administration less than once per month. Injection users also tended to administer the drug cnly once per episode. However, repeated injections were usually self-administered once per hour until a desired level or period of intoxication was achieved.

PATTERNS OF USE

The five patterns of use previously designated by The National Commission on Marihuana and Drug Abuse (1973) will be used for discussion here.

Experimental Use

Six subjects (60 percent) of the Intranasal Group and one (8 percent) of the Injection subjects were classified as experimental users and engaged in short term, nonpatterned trials of ketamine with varying intensity and a maximum frequency of 10 times or less in their entire drug history. These users were motivated by curiosity about ketamine (or its advertisement as a different type of drug such as "Green" or "K") and a desire to experience the anticipated effects of euphoria and hallucinations. Their use was generally social and among close friends or intimate others. Most subjects enjoyed the experience but did not express a desire to continue regular use because of the street myth that "something that strong must have some harmful effects on the brain." Other subjects desired to repeat the self-administration but found cost to be prohibitive (the drug is in short supply).

Social-Recreational Use

In the Intranasal Group, four subjects (40 percent) were classified as social-recreational users. Ten subjects (77 percent) in the Injection Group were also classified in this way, but three of these subjects (23 percent) engaged in episodes of more frequent use (see below). In general, social-recreational use occurred more regularly than experimental use and was primarily motivated by individuals seeking to share with others an experience they judged to be pleasant and fun. Such users describe their ketamine use as "absolutely safe" and "better than LSD." The set and setting for recreational use parallels that observed with other more conventional hallucinogens. The Intranasal users tended to employ low dosages (probably less than 50 mg) and found the experience to be similar to cocaine but more "trippy." This comparison to cocaine is probably related to ketamine's cocaine-like effects on vascular adrenergic neurons (Nedergaard 1973). The use of the term "trippy" refers to ketamine's hallucinatory and dissociative effects.

Injection users tended to employ sufficient dosages to produce the "psychedelic" effects. When asked to rank all recreational drugs in terms of potency, all social-recreational ketamine users ranked ketamine as the most potent hallucingen and 71 percent rated it as the hallucinogen of choice. The remaining subjects were equally divided between LSD and psilocybin mushrooms as their hallucinogen of choice. When asked to rank all drugs in terms of general recreational preference, Intranasal Users ranked cocaine first, while Injection Users ranked LSD first. Ketamine was consistently described in several ways which contributed to the maintenance of social-recreational patterns of use:

1) Ketamine was perceived by users to be a safe, non-toxic, potent hallucinogen with a short duration of action and few adverse reactions or bad trips.

2) Ketamine was perceived by most users as the only hallucinogen that did not produce anxiety or fear reactions.

3) Ketamine was considered to have unique euphoric-hallucinogenic properties that enabled a user to experience, with varying dosages, effects similar to either cocaine, amyl nitrite, phencyclidine, or LSD.

4) Ketamine was considered to be a glamorous avant-garde drug and had associations with cotemporary folk heroes of high status (see Duncan 1976).

Circumstantial-Situational Use

Only two subjects in the Injection Group (15 percent) engaged periodically in circumstantial-situational use, defined as a task-specific, self-limited use which was variably patterned, differing in frequency, intensity and duration. This use was motivated by a desire to explore new states of consciousness and work through personal problems. Such use is similar to that of ketamine in experimental psychotherapy situations (Khorramzadeh and Lofty 1973).

Intensified Drug Use

Only two subjects in the Injection Group (15 percent) engaged in intensified use characterized by long term patterned use of at least once per week for several months. Such use was motivated chiefly by a perceived need to achieve relief from a persistent problem or stressful situation or a desire to maintain a certain self-prescribed level of intoxication. Nonetheless, users here still referred to their use as "experimental" in the sense that they were exploring new altered states.

Compulsive Drug Use

Only one subject (8 percent) in the Injection Group characterized herself as a compulsive ketamine user with high frequency and high intensity levels of relatively long duration. This user admitted to both psychological and physical addiction to the drug, although this latter claim could not be substantiated. Indeed, she was able to "withdraw" repeatedly from the ketamine use which continued intermittently for several years.

PHENOMENOLOGY AND INCIDENCE OF INTOXICATION EFFECTS

The acute physiological and psychological effects reported by ketamine users did not differ substantially between the Intranasal and Injection Groups. Therefore, the users are combined (total N = 23) in discussion here. In general, most users recognized that they were using a hallucinogen, and considered the hallucinogenic and psychotomimetic properties to be positive effects. This attitude (set) contrasts sharply with most phencyclidine users who only recognized that they were using an intoxicant similar to marihuana, which is commonly not considered a hallucinogen in street usage.

Ketamine users repeatedly sought and experienced a number of positive effects, including: floating sensations and dissociation (87 percent), stimulation (83 percent), hallucinations (78 percent), increased cognitive or mental associations (74 percent), euphoria (26 percent), and transcendental or religious experiences (17 percent). Despite the widespread beliefs among users about the lack of adverse reactions, a number of untoward effects were also reported: ataxia (100 percent), slurring of speech (70 percent), dizziness (61 percent), mental confusion (35 percent), hyperexcitability (26 percent), unpleasant imagery (26 percent), blurring of vision (17 percent), negative hallucinations, or the inability to see things that were really there (17percent), decreased sociability (17 percent), anxiety (13 percent), nausea (13 percent), insomia (13 percent), and decreased sexual motivation (9 percent). Interestingly, one subject also experienced several episodes of psychomotor seizures as a result of acute intoxication.

Taken together,ketamine users experienced more negative effects than positive effects as a result of acute intoxication. Nonetheless, they continued to rate the overall experience as positive and rewarding.

The long term effects resulting from ketamine use are similar to those reported for many other hallucinogenslike LSD. Typically, the ketamine users claimed a chronic elevation of mood (43 percent), deeper insights into self and others (35 percent), and positive changes in attitudes personality (17 percent). The undesired long term effects included: flashbacks (57 percent), attentional dysfunction (22 percent), and decreased sociability (9 percent).

Overall, long-term effects appeared equally divided between positive and negative experiences.

HALLUCINATIONS

Of the phenomena reported above, the hallucinations appeared to be conspicuous as both positive effects resulting from acute intoxication and as important determinants of positive/negative long term effects. Therefore, the ketamine hallucinations among these non-medical users were the object of concentrated examination and study. In general, the nature of ketamine hallucinations in recreational users was similar to that reported in both surgical and experimental subjects (e.g., Collier 1972; Siegel and Jarvik 1975). One subject from the Injection Group described her prototypical hallucinations in a session that she tape-recorded for the author:

> I see Mexico City when I close my eyes. Crazy. I've never been there before. Now it's just black. It reminds me of a cave. I see people moving about in some sort of kaleidoscope pattern. I don't know where I am. (Laughter) The crowd of people are all having a good tine and they're laughing. My sister has got her Sunday blue dress on, although she's always dressed in black. I don't recognize anyone except her and her husband. Now they're gone. They disappeared. Now I just see commercials from TV and lots of geometric patterns. There's someone's stereo hanging on the wall. (Laughter) I feel a little childish. Happy. Very happy. (Laughter) Now I see kitty cats. Striped ones like out of a child's coloring book.

Another Injection subject described a similar experience, also tape-recorded for the author:

> I see flowers. All colors, blue and green and purple, yellow. And now a weird looking nightclub. Now stars. Everything happening very fast.....vegetables, pictures, a house, a pinwheel, there's a man sitting on a chair. It's just like a movie or a dream. There's an igloo and a tepee. And some more flowers. (Laughter) Now I feel like I'm in church. Really, it's really a church. My tongue hurts. And in the church is a tiny dot in the middle and some black space and then from the middle comes a white light. Surrounded by flowers like lilacs, rippling like in the wind. And pink flowers and white picket fence. Now I see Jesus. And I see a man and a woman kissing. Now I see white flowers and just green leaves. And there is an old man on the other side and he is waving his hand and he's gotasuitonandahat. That must be God. Now I see a little girl. (Laughter) That's me. She's laughing. This is all very clear. I can even see their features and everything.

Even Intranasal users experience similar, albeit weaker, hallucinations as exemplified by one subject's report:

> The first thing that happens when I snort Green (ketamine) is that I start to get speedy like with coke (cocaine). I feel a rush of good feelings, almost euphoric. Then things get a little blurry. I feel like I'm floating and sometimes dizzy. But I usually lie down and float along with the trip. When I close my eyes I see the "retinal circus" that Tim Leary described with kid (LSD)--lights, colors, patterns, even

> cartoons and memory pictures. If it's dark in the room and I open my eyes I can sometimes project things onto the wall or ceiling. But most of the time I just lie there thinking great thoughts and solving lots of problems. It's a lot like nitrous oxide only it's a more intense body trip as well. When you snort it you come down very quickly.

As suggested above, experienced users of ketamine can learn to utilize the state of intoxication for personal growth and exploration. This use is similar to that underlying long term recreational use of other hallucinogens, and Lilly et al. (unpublished manuscript) describe the unique aspects of ketamine in this regard.

> In our group we symbolize this by saying that this chemical induces a state in which you live in a well of neutral reinforcement. Typical tasks are simplified and made more efficient, condensed, abstracted, and the nonsense removed from the computations involved in carrying them out. Mental processes in a similar way sharpen out. It looks as if the contrast enhancement of such as edges, colors, thoughts, ideas and so forth is forthcoming. Colors seem brighter and yet more meaningful. Objects contain their own meanings. People are read very readily and with great ease and evaluated in their current state anrd dealt with in the most efficient and energetic manner possible. After some weeks of training to get through the initial phases of the emergence symptoms so-called, these states occur. The subject learns to centrally control, integrate and use the neutral energy afforded by the ketamine and becomes that which he potentially could become otherwise without the chemical at his best performance (p.4).

III. OVERVIEW

The nonmedical use of phencyclidine (PCP) and ketamine has been examined in four populations of recreational users. The first population sample consisted of 319 Adult users of PCP while the second population sample consisted of 20 Juvenile users of PCP. Both groups used PCP primarily by smoking in social-recreational patterns and settings. However, Juveniles tended to be more intensified users than Adults, many of whom were only experimenting with the drug. PCP was viewed as a potent hallucinogen by users, who tended to titrate dosages in order to achieve desired levels of stimulation, dissociation, and inebriation. Such positive effects were achieved in approximately 60 percent of the intoxications. Despite the fact that negative effects such as perceptual disturbances, dysarthria, and hyperexcitability were common in nearly all intoxications, a substantial number of individuals maintained continued use of and preference for the drug. These patterns of use are probably related to the dissociation and estrangement from self and others induced by PCP, as well as the drug's euphoro-hallucinogenic properties.

!The third population sample consisted of 10 Intranasal ketamine users while the fourth population sample consisted of 13 Injection users of ketamine. Use of ketamine was primarily experimental or social in nature and the drug was viewed by users to be a safe, potent hallucinogen with a short duration of action and few if any adverse effects. Ketamine users tended to titrate their use in order to achieve desired effects of dissociation, stimulation, hallucinations, and transcerdental experiences. Despite the users' beliefs that the drug was totally safe, negative effects were reported; these included ataxia, dizziness, mental confusion, and hyperxcitability.

Long term intensified use of PCP tended to be associated with abnormal personality profiles indicating the drug's psychotomimetic actions. Long term use of ketamine was marked by a high incidence of flashbacks as well as attentional dysfunction. Nonetheless, recreational users of both drugs tended to experience generalized feelings of well-being, heightened perceptual sensitivity, and positive and rewarding experiences which reinforced and maintained drug use. Some tendency toward transient psychosis was noted in the PCP groups, while the ketamine users manifested some decreased sociability with no concomitant personality changes as measured by standard psychometric tests. An important caveat is that these effects are neither uniformly negative nor uniformly predictable. The number of variables affecting their production is presently unknown.

ACKNOWLEDGMENTS

The author thanks Dr. Murray E. Jarvik for numerous helpful services in the research and preparation of this study. The author is indebted to Ada Hirschman for superlative research assistance. Arthur Stickgold provided valuable research materials.

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Chapter 7

Epidemiology of Multiple Drug Use with Special Reference to Phencyclidine

J. Fred E. Shick, M.D.

Recently we have witnessed growing concern about the illicit use of phencyclidine (PCP) among this nation's youth. Epidemiological data has been difficult to assemble quickly, since most surveys either have included PCP within the category of hallucinogens" or have anitted questions about it altogether (Johnston 1973; Abelson and Fishburne 1976; O'Donnell et al. 1976). The primary source of descriptive data, useful in estimating the range of usage patterns and adverse reactions, has been studies of youth in crisis from PCP use -- usually samples from hospital settings and drug abuse programs (Burns et al. 1975; Burns and Lerner 1976; Fauman et al. 1976; Fauman et al. 1975; Linden et al. 1975; Tong et al. 1975).

The focus of my research has been to develop a fieldwork methodology to locate and gain access to heavy, multiple drug-using youth at their congregation sites. These youth -- generally the underemployed and undereducated 16 to 26 year old age group -- are at risk for a variety of adverse outcomes, including progression to intensified drug use, experimentation with intravenous administration, as well as acute and chronic adverse drug reactions My research has borrowed concepts and methods from participant observation fieldwork methodologies (Becker 1970; Habenstein 1970; Weppner 1977) and the work of Hughes and coworkers with heroin addict communities in Chicago (Hughes 1977; Hughes and Crawford 1972; Hughes et al. 1971; Hughes and Jaffe 1971; Hughes, Senay, and Parker 1972).

Our previous studies (Shick, Dorus, and Hughes 1978; Shick and Wiebel 1978) utilized fieldwork techniques to identify sites popularly known as "hangouts" where youthful multiple drug users congregated to buy, sell and use drugs. We also used these techniques to study intensively the social organization and activities of groups of youth at certain sites. Particularly remarkable were the relative geographic stability of these locations during the warmer months, the regularity with which particular groups frequented a given site, the preponderance of males, and the recreational and social quality of the groups' activities, including drug use. These studies suggested that youthful drug user hangouts may be conceptualized as "neighborhood" or "regional." Neighborhood hangouts were frequented by smaller numbers of visitor who lived in the immediate neighborhood, attended the same high school, knew one anothers' brothers and sisters,and were from similar ethnic and socioeconomic backgrounds. Drugs available at these sites appeared to be limited in both quantity and variety by the small number of dealers a who generally residents of the neighborhood. By contrast, regional sites were characterized by large number of visitors who came from an extremely wide area and were not organized into cohesive friendship groups on consisting of long-term neighborhood friendships established during grade school and high school. Regional sites appeared to attract the heaviest drug users and dealers, and a wide range of drug types were regularly available. Regional sites were well known to most visitors to the neighborhood locations but were avoided by them and visited only occasionally when drugs were available at their usual neighborhood hangouts. Observation and informal interviews suggested that violence among individuals and groups was more common at regional sites, particularly those of wide social and economic diversity, and areas frequented by delinquent gangs.

This work demonstrated that fieldworkers who themselves had been multiple drug users and who were residents of and regular visitors to the area under investigation were able to locate and characterize drug user congregation sites and could be trained to gain access to users to perform epidemiologic field research activities. We were fortunate in these studies to have the foresight to include in our fieldinterviewsa separate category of questions about drugs generally analyzed to contain phencyclidine (PCP).

In this paper we report the epidemiological drug use data collected from regular visitors to two regional congregation sites in the Chicago area: (1) the largest congregation and drug distribution site in the south Chicago suburbs, active during warm weather, and (2) the largest urban congregation and drug distribution on the near month side of Chicago, which was active throughout the year.

METHODS

The field team for each site consisted of two fieldworkers who were regular members of the drug-using community being stuied and who themselves occasionally used illicit drugs. They were trained in fieldwork and interview techniques andregularly supervised by the research sociologist and the author. A more detailed discussion of the recruitment procedures, selection criteria, and training for fieldworkers is presented in a forthcoming report.

We began by asking the fieldworkers for each location,who were familiar with the area, to identify all known hangouts for multiple drug users. Fieldworkers then made several visits to each site on different days at different hours, and in fieldnotes they estimated the number of visitors present, their age range, and other demographic characteristics, the drugs available, and whether visible dealing or use occurred. They discussed the local drug scene with individuals they met at these sites and asked about additional dtug user hangouts, which then were visited. The research sociologist and the author verified the fieldworkers' observations by personal visits and informal interviews on a regular basis.

From this data, early in the summer of 1975, we identified for intensive study, the largest and most popular congregation sites in each area. Informal interviews with regular visitors to these and other locations confirmed fieldworkers' reports that these sites were the primary hangouts for the heaviest multiple drug users and dealers from surrounding areas.

At the suburban forest preserve (Site one) during July through November, 1975, fieldworkers administered structured field interviews detailing demographic characteristics, drug-using habits, and service needs to 71 subjects who were selected by word-of-mouth chains of referral from approximately 100 regular visitors to this site. The interviews were conducted at the site in an area away from the greatest activity or in the fieldworker's car.

At the urban congregation site (Site two) we rented a field office in the area, and there fieldworkers administered the same interviews to 236 subjects similarly selected from approximately 300 regular visitors, between July 1975 and December 1976. Each subject was paid $5 for his participation in the interview.

To minimize the effect of seasonal variation in drug availability, popularity, and visitor attendance, in this paper we compare epidemiological drug use data from Site one with that from 118 of the 236 subjects selected from site two who were interviewed during the same period -- July through November 1975.

RESULTS

Intensive Study Sites

The south Chicago suburbs include approximately 40 incorporated cities and towns ranging in population from 1,500 to 60,000 in the highly industrialized 180 square mile area. Most of the households consist of white, blue collar, working class families, less than 1 percent are nonwhite, and less than 10 percent are defined as white collar. The site of intensive study was a forest preserve visited in the late afternoon and evening hours during good weather by 100 to 300 youth, who arrived in cars from an extremely wide geographic area. Drug dealing and use was open and uninhibited,and regular police patrolling seemed to have little effect (Shick and Wiebel 1978). The drugs available at this site varied with the attendance; on slow days only marihuana was available, but on busy days a wide variety of drugs, including occasionally heroin, was sold.

The near north side of Chicago is a heavily populated area surrounded by affluent whites along Lake Michigan and Latino and

TABLE 1

DEMOGRAPHIC CHARACTERISTICS OF THE
STUDY SAMPLES COMPARED

Age (Years)	Forest Preserve Sample (N=71)			Urban Sample (N=118)		
	Males	Females	Total	Males	Females	Total
< 18	17%(9)	72%(13)	31%(22)	26%(26)	16%(3)	25%(29)
18-20	34%(18)	17%(3)	30%(21)	42%(42)	53%(10)	44%(52)
> 20	49%(26)	11%(2)	39%(28)	31%(31)	32%(6)	31%(37)
Total	75%(53)	25%(19)	100%(71)	84%(99)	16%(19)	100%(118)

	Forest Preserve Sample	Urban Sample
Mean Age	19.9 years	20.9 years
Modal Age	17 years	18 years
Median Age	19.2 years	18.9 years
Ethnicity		
White	98% (70)	82% (97)
Black	2% (1)	8% (9)
Latin	(0)	8% (9)
other	(0)	2% (3)
Religious Training		
Catholic	52% (37)	50% (59)
Protestant	28% (20)	25% (29)
Jewish	1% (1)	7% (9)
other	12% (8)	12% (14)
None	7% (5)	6% (7)
Marital Status		
Single	86% (61)	89% (105)
Married or Common-law Partner	13% (9)	1% (1)
Separated	1% (1)	1% (1)
Divorced	(0)	9% (0)
Children	11% (8)	18% (21)
Education		
currently Attnd'g School	34% (24)	14% (17)

TABLE 1 (cont'd.)

DEMOGRAPHIC CHARACTERISTICS OF THE STUDY SAMPLES COMPARED

Age (years)	Forest Preserve Sample (N=71)	Urban Sample (N=118)
Last year of School Completed		
8th Grade or less	1% (1)	15% (18)
9th	10% (7)	19% (22)
10th	23% (16)	19% (22)
11th	34% (24)	16% (19)
12th	20% (14)	20% (23)
Some College	13% (9)	10% (12)
Grad'd College	(0)	1% (2)
High school Equivalency Exam	3% (2)	8% (9)
Currently Employed	25% (18)	27% (23)
Area Grew up (to age 13)		
Chicago		57% (67)
Chicago Suburban Area		7% (8)
Other Part of Illinois		5% (6)
Out of state		30% (35)
No Answer		1% (2)
Employment Status of Family's Major Provider		
Higher Exec., Professional	2% (1)	5% (6)
Lesser Managerial	34% (22)	9% (10)
Adm'n., Small B'sns.Owner	9% (6)	11% (13)
Clerical Technical	34% (22)	14% (17)
Skilled Manual	8% (5)	19% (22)
Semi-Skilled Man'l.	13% (8)	16% (19)
Unskilled	(0)	12% (14)
Public Assistance, Orphan	(0)	14% (17)

and lower class whites to the northwest.It is also a popular shopping and nightlife district among young singles. The several drug user hangouts here were within walking distance from One another and attracted drug users from a wide area. These hangouts were an integral part of an urban neigborhood and were active throughout the winter months, in contrast to the isolated sites such as parks, beaches, or forest preserves, which were active only during warmer weather. Furthermore, the urban site attracted diverse types of multiple drug users various ethnic and socio-economic backgrounds and numerous adolescent runaways.Our sample included regular intravenous users of amphetamine and heroin who frequented the pool hall, intravenous experimenters using various drugs, and a large number of daily or weekend users of pharmaceuticals, psychedelics, PCP, alcohol, and marihuana who "hung out" regularly at the restaurants. Subjects' occupation ranged from legal employment to careers of crime: illegal activities included drug dealing, male and female prostitution, pimping, shoplifting, burglary, and con games. The full range of drugs was regularly available from many sources including many of the youth themelves, several large quantity dealers who lived in the nearby hotels,and about five pathological prescribers.

Table one displays the demographic characteristics of the two samples. Both samples included substantially more males than females, which accurately reflected the composition of the regular visitors, verified by fieldwork. In contrast to the suburban forest preserve sample, there were more nonwhite subjects and a greater number of older subjects among the urban sample.

Subjects from the suburban forest preserve sample had grown up near the area where they presently lived. By contrast, only 64 percent of the urban sample subjects had grown up in Chicago or its suburbs, and 30 percent had grown up outside the state of Illinois (5 percent had grown up in Illinois outside the Chicago metropolitan area). A greater proportion of urban samples subjects had dropped out of school (many during grade school or early high school), had left home at an early age, and were no longer living with parents (78 percent). Two-thirds of the suburban sample and 86 percent of the urban sample were no longer attending school, and threer-quarters of both samples were unemployed.

Epidemiologic Data

In contrast to the epidemiologic assessment of heroin addiction (Hughes 1977; DuPont and Greene 1973; Greene et al. 1974) the study of trends and patterns of drug use among multiple drug users is complicated by the wide variety of drug types used, the various definitions of "multiple drug use" (Elinson and Nurco 1975; Single, Kandel, and Faust 1974), and the questionable purity of many of these drugs (Cheek, Newell, and Jaffe 1970; Kealy and Webber 1975). The drug use reported by subjects reflects the alleged content and must be interpreted in the light of the prevalence of misrepresentation and the considerable variability in potency of some drug types.

In our analysis, the drug category representing phencyclidine (PCP) is labeled "dust." Fieldworkers were trained to question users in detail about substances which might have contained PCP. Preliminary fieldwork and results from the Chicago Drug Analysis Network indicated that in Chicago during 1975-1976 the preperations most likely to contain a substantial amount of phencyclidine were marketed under the street names "PCP, dust, angel dust, TIC, TAC, and THC." Thus, these street names were incorporated into the structured field interview to obtain the subject's self-report of PCP use.

Results published by PharmChem laboratories during the period of our study were consistent with the results from the Chicago Drug Analysis Network (Helisten 1977; Perry 1977; Rainey and Crowder 1974; Kealy and Webber 1975). (Four percent of subjects from Site one and 11 percent from Site two reported having utilized the services of a drug analysis service.) Practically 90 percent of the drugs marketed as PCP, dust, angel dust,THC,TIC, and TAC contained phencyclidine, and drugs sold as amphetamines, cocaine, or psychedelics had a much higher misrepresentation rate. The amount of PCP in samples varied from less than 5 percent to almost 100 percent. Generally less than 10 percent of the drugs sold under these street names were analyzed to contain no identifiable drug. Other drugs occasionally found in admixture included small quantities of cocaine, and psychedelics such as LSD or MDA.

Although reports from the West Coast (Burns and Lerner 1976) suggest a recent increase in smoking materials represented as marihuana but adulterated with PCP, fieldwork data indicated that in Chicago during thetimeperiod studied, very seldom did this type of use occur -- PCP was rarely marketed surreptitiously. Although some users thought they were getting cannabinol when buying "THC," the majority of subjects, most of whom were experienced and "street wise" users, knew of -- and sought -- the "animal tranquilizer" contained in these substances.

Incidence (First Use)

Incidence data, the number of "new cases" in a particular year, were derived from questions about season and year of first use, and results from each sample were remarkably similar. At each site first experimentation with every drug type (except heroin and cocaine; see below) was declining due to the artifact of "saturation." Incidence is a one-time occurrence, and by 1975, from 70 to 90 percent of subjects in both samples had tried every type of drug surveyed except codeine, cocaine, heroin, methadone and solvents, seriously depleting the pool of those still eligible for "first use" (Hughes, Schaps, and Sanders 1973).

Data from both sites indicated that among every age group (<18 years; 18-20 years; > 20 years) peak incidence of PCP use occurred more recently than any other drug type.

At Site one, peak incidence for sedative-hypnotics (1971-1972) and dust (1973-1974) was separated by two years. Among younger subjects, peak incidence of psychedelic use occurred two years before peak incidence of dust; among older subjects, peak psychedelic incidence occurred four years before peak incidence of dust.

At Site two, among subjects less than 18 years old, incidence for dust peaked in 1972 and again in 1975. This bimodal curve may be an artifact or may represent local variations in popularity, availability, or sample selection factors (Richman and Abbey 1977). If this bimodal incidence is considered artifactual and the curve is interpolated, peak incidence of PCP use among younger subjects appears to have occurred very recently, 1974-1975, approximately one year following the peak incidence of sedative-hypnotic use, and two years following the peak incidence of psychedelic experimentation. Among the 18 to 20 year olds at Site two, peak incidence of PCP use occurred between 1973 and 1974, again approximately one to two years following the peak incidence of sedative-hypnotic use, and one to two years following peak incidence of psychedelic experimentation. Among subjects over 20 years old at site two, peak incidence of dust use occurred about 1972; peak incidence of sedative-hypnotic, amphetamine, and psychedelic use occurred between 1967-1969.

Among subjects less than 18 years old at both sites, heroin and cocaine use displayed a recent rising incidence during 1972-1974. Among the urban sample (Site two) a similar rising heroin incidence was observed among the 18-20 year olds; among subjects older than 20 years at this site, heroin incidence peaked between 1970-1972.

Whether the mean, modal, or median age that subjects had first tried each drug type was inspected, results from each site suggested that the drugs subsumed under the category of "dust" were first tried relatively late in the sequence of use. Generally subjects had tried alcohol, marihuana, (solvents, glue, and codeine in a minority), sedative-hypnotics, amphetamines, and psychedelics prior to their first trial of dust. Trial of opiates, when it occurred, appeared to follow trial of dust. Among older subjects (Site two) the age at which they first tried dust was most closely associated with, and generally followed, their first trials of sedative-hypnotics and amphetamines. The younger users' first trials of dust were more closely associated with subjects' first trials of psychedelics and amphetamines which followed their first trials of sedative-hypnotics.

Results suggested that younger users who regularly frequent regional drug user hangouts such as these may be more likely than older users to try a variety of drugs shortly after their initial trials of marihuana. Data from both sites suggested that in contrast to subjects 18 years or older, whose first use of each drug was more widely spaced in time, most of the younger subjects had tried several different drug types within a brief period of six to 18 months. This tendency of younger users to try "any drug available" was also characteristic of the subjects we studied (Shick, Dorus, and Hughes 1978) on the far north side of Chicago (frequenting a much smaller, neighborhood site) and is consistent with our impressions from work in adolescent drug treatment programs. Whether adolescent experimentation with a variety of substances within a brief span of time reflects a different attitude about drug use among younger adolescents and is predictive of eventual heavy use deserves further study.

Prevalence, Remission, and Frequency of Use

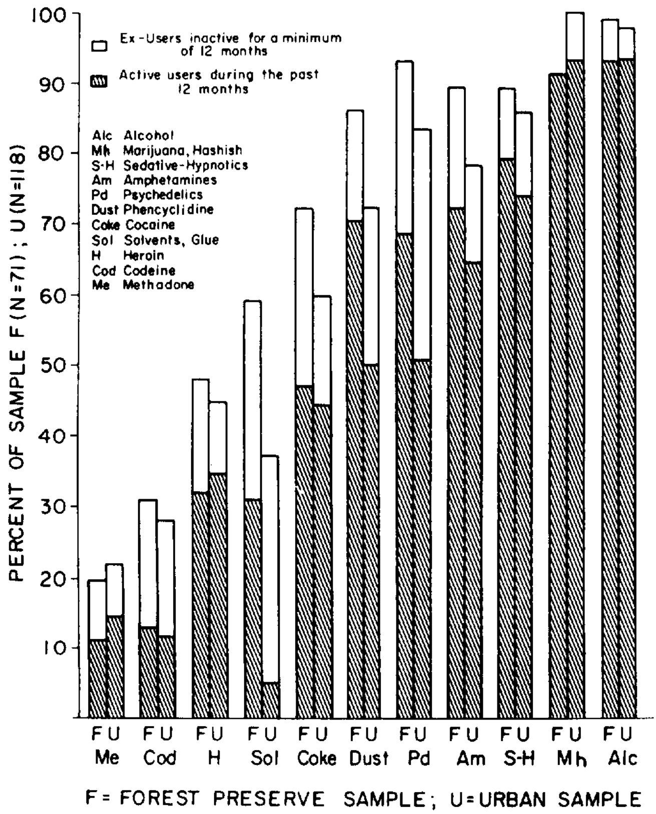
In Hughes and Crawford's work (1972) in heroin-copping areas, heroin prevalence data was relatively easily collected by ex-addict fieldworkers. Weekly logs of the number of addicts visiting a copping area reflected prevalence of active addiction because most addicts must make daily visits in order to obtain drug supplies and to avoid the distress of withdrawal symptoms. At youthful multiple drug user sites prevalence of drug use must be determined by self-report, since the majority of users are not physically dependent. There is a recreational quality to drug use at these sites, and a visitor's mere presence does not indicate what drug(s) s/he may be using.

Computer analysis determined the prevalence, remission and frequency of use of each drug type for each of the two samples from self-reports of frequency of use during the 12 months prior to interview.

Figure one compares the prevalence and remission rates for the two samples. Prevalence of drug use was defined as the percentage of subjects who had used a particular drug type at least once during the prior 12 months. Remission was defined as the percentage of subjects who had tried a given drug type but had not used the drug during the 12 months prior to interview. The percentage of subjects reporting ever having used each drug type is the sum of the prevalence percentage plus the remission percentage (see figure one).

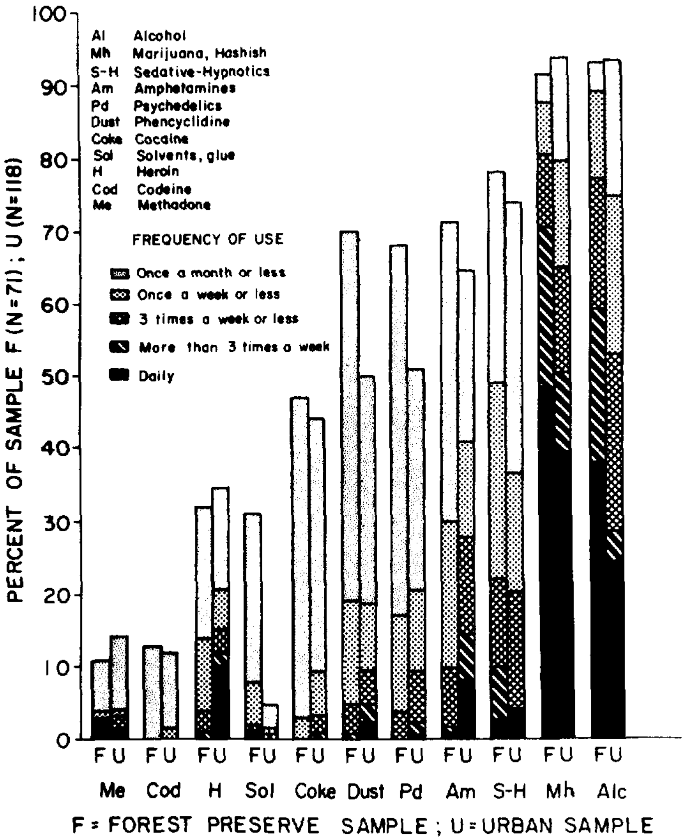
Marihuana and alcohol displayed the greatest prevalence of use and least remission among both samples. In rank order, sedative-hypnotics, amphetamines dust, and psychedelics registered the next greatest prevalence rates at both sites: prevalence rates for these drugs were consistently greater among subjects from the suburban forest preserve than among subjects at the urban site. At both sites the magnitude of the remission rates for these drugs was the reverse order of their prevalence: psychedelics, dust, amphetamines, and sedative-hypnotics, in that order. The prevalence of cocaine use was approximately the same for subjects from both sites, but the remission rate for cocaine was slightly greater at the suburban forest preserve than at the urban site. The same was true for heroin. The slightly lower remission rates for heroin and cocaine among the urban sample may reflect the greater number of heroin addicts in the urban sample, and possibly their concomitant use of cocaine. Solvents and glue had greater remission rates than any other drug type among both samples; however, the prevalence of solvent use was much greater at the suburban forest

FIGURE 1



PREVALENCE AND REMISSION RATES OF TWO SAMPLES COMPARED: F = 71 REGULAR VISITORS TO A CHICAGO SUBURBAN FOREST PRESERVE DRUG USER SITE, SUMMER 1975; U= 118 REGULAR VISITORS TO A CHICAGO URBAN DRUG USER SITE, SUMMER 1975.

FIGURE 2



FREOUENCY OF DRUG USE DURING THE 12 MONTHS PRIOR TO STUDY OF TWO SAMPLES COMPARED: F = 71 REGULAR VISITORS TO A CHICAGO SURBURBAN FOREST PRESERVE DRUG USER SITE, SUMMER 1975; U = 118 REGULAR VISITORS TO A CHICAGO URBAN DRUG USER SITE, SUMMER 1975 preserve than at the urban site. The high remission rates reported for psychedelics may reflect users' unpleasant experiences with these drugs, indicated by the large number of adverse reactions reported for psychedelics. In fact, remission rates for psychedelics, dust, amphetamines, and sedative-hypnotics approximate the rank order of the number of adverse reactions reported for them.

Figure two compares the frequency of use of each drug type for the two samples. Frequency data was obtained by asking each subject to estimate the number of times during the past 12 months s/he had used a particular type of drug and whether her/his use occurred on a periodic basis, for example, daily, or on weekends. Because these subjects reported high rates of use, the following frequency intervals were calculated: use of the drug once a month or less; more than once a month to once a week; more than once a week to three times a week; four times a week to almost daily use;and daily use.

Although prevalence of marihuana and alcohol use was approximately the same for the two samples, a greater number of subjects reported daily use of these two drugs among the suburban forest preserve sample. Although the prevalence rates for sedative-hypnotics, amphetamines, dust, and psychedelics were lower among subjects in the urban sample, there were more daily users of amphetamines (ten subjects), sedative-hypnotics (five subjects), dust (three subjects), and psychedelics (one subject) among the urban sample.

Although approximately the same percentage of subjects at both sites had used dust and psychedelics more than once a month, there was a greater number of heavier users among the urban sample than among subjects at the suburban forest preserve. Frequency of heroin, amphetamine, and cocaine use was greater among the urban sample, reflecting the greater number of near-daily intravenous users among these subjects (see table two).

There are numerous definitions of multiple drug use (Elinson and Nurco 1975). We used a method modified from that described by Hughes, Schaps, and Sanders (1973) to assess the number of drug types (excluding alcohol and marihuana)used by each subject at least once during the 12 months prior to interview. The results are displayed in table three. Sixty-six percent of the subjects from Site one and 44 percent from Site two had used between four and six different types of drugs. There was a tendency for the 15 to 17 year olds among the forest preserve sample to have used a wider variety of drugs than older subjects; among the urban sample, this tendency was displayed among the 18-20 year olds. We compared the variety of drugs used by both samples with a sample of 216 heroin addicts entering treatment (Senay and Shick 1976) and a 1970 sample of 13,412 Chicago suburban high school students (Hughes, Schaps, and Sanders 1973). Results indicated that both field samples of youthful multiple drug users had used a much wider variety of drugs with greater frequency than did heroin addicts entering treatment or the high school students.

TABLE 2

MEAN FREQUENCY OF DRUG USE DURING THE PAST TWELVE MONTHS AMONG ACTIVE USERS OF TWO SAMPLES COMPARED

Mean Frequency of Use During the Past 12 Months*

Drug Type	Al.	Mh.	Sol.	Cd.	S-H	Am.	Co.	Dust	Pd.	H.	O.O.	Mth.
F	231.5	264.3	26.7	3.7	60.7	37.5	5.1	22.2	16.1	28.9	10.3	96.0
U	148.6	206.3	22.0	8.6	57.7	102.1	17.3	48.1	36.5	133.5	42.6	59.9

F = Forest Preserve Sample (N=71)
U = Urban Sample (N=118)

Key to Abbreviations

Al.=Alcohol;Mh.=Marihuana; Sol.=Solvents; Cd.=Codeine; S-H= Sedative-Hypnotics; Am.=Amphetamines; Co.=Cocaine; Dust=Phencyclidine; Pd.=Psychedelics; H.=Heroin; O.O.=Other Opiates; Mth.= Methadone.

* Includes only "active users," that is, subjects who used at least one drug one time during the 12 months prior to interview. Frequency is expressed as the mean number of days used per year over the past 12 month interval.

TABLE 3

VARIETY OF DRUG USE* OF TWO SAMPLES COMPARED

Variety of Use Category		Suburban Forest Preserve Sample		Urban Sample	
		N = 71		N = 118	
		%	N	%	N
Nonuser		0	(0)	0	(0)
Alcohol only		0	(0)	1	(1)
Marihuana and/or Alochol		1	(1)	6	(7)
One of		6	(4)	13	(15)
Two of	solvents	11	(8)	15	(17)
Three of	Sedative-Hypnotics amphetamines	8	(6)	11	(13)
Four of	Dust Phychedelics	20	(14)	17	(20)
Five of	Cocaine Codeine	23	(16)	18	(21)
Six of	Heroin Methadone	23	(16)	9	(11)
Seven of	Other Opiates	4	(3)	5	(6)
Eight of		4	(3)	3	(3)
None of		0	(0)	2	(2)

* Adapted with modification from a method devised by Hughes, Schaps, and Sanders (1973). Subjects included have used a drugtype at least once during the 12 months prior to interview.

Intravenous Drug Use

Intravenous experimentation is of particular concern since it appears to signify a "quantum jump" in drug using habits and attitudes, often heralds a change in friendship group, increases the primary drug reinforcement effects (the "rush"), places users at risk for adverse medical consequences such as serum hepatitis, and is a precursor to heroin (or intravenous amphetamine) addiction. Furthermore, as deAlarcon (1971) discussed, the injecting ritual itself is communicable."

At Site one, 40 (56 percent) of the 71 subjects, including six of the 22 subjects 15 to 17 years old, had experimented at least once with the intravenous route of administration. The diversity of drugs injected was the same for every age group. In rank order, the drugs most frequently injected were opiates (generally heroin), amphetamines, dust, cocaine, psychedelics, and sedative-hypnotics. Intravenous experimentation was more common among males (66 percent) than among females (22 percent); intravenous amphetamine and cocaine use was more common among subjects 18 years or older than younger subjects.

The urban sample (Site two) included a larger nunber of daily intravenous users of heroin and amphetamines. Sixty-nine (58 percent) of the 118 subjects (including eight of the 29 subjects less than 18 years old) had experimented at least once with intravenous injection. In contrast to the suburban forest preserve sample, intravenous drug use was more common among the females (84 percent) than among males (54 percent). In rank order, the drugs most frequently injected (of those who had ever tried the drug itself) were heroin (81 percent), other opiates (29 percent), amphetamines (52 percent), cocaine (27 percent), sedative-hypnotics (25 percent), "dust" (23 percent), and psychedelics (18 percent). The relatively greater percentage of subjects at Site two who had tried cocaine and sedative-hypnotics intravenously than at Site one my reflect the slightly older age of the sample, the association of intravenous cocaine and heroin use among heroin addicts, or the use of intravenous sedative-hypnotics to substitute for heroin when unavailable or to "come down" from amphetamine intoxication among habitual users.

Adverse Reactions

Table four displays the total number of adverse reactions reported by subjects from each site. There were a greater number of adverse reactions reported at the suburban forest preserve than at the urban site, but this was a function of the larger number reportedly due to alcohol at site one.

Table five displays the adverse reactions reported by subjects from Site one. Fifty-six percent of the 127 adverse reactions reported were of a physiological nature, generally nausea, headaches, and vomiting, and 41 percent of these were reportedly due to alcohol. "Bad trips," predominantly acute anxiety reactions or unpleasant

TABLE 4

NUMBER OF SELF-REPORTED ADVERSE REACTIONS OF TWO SAMPLES COMPARED

	Including Alcohol		Excluding Alcohol	
Number of Adverse Reactions	Forest Preserve Sample	Urban Sample	Forest Preserve Sample	Urban Sample
	Subjects % N	Subjects % N	Subjects % N	Subjects % N
None	10%(7)	34%(40)	20%(14)	35%(42)
one	31%(22)	35%(42)	39%(28)	35%(41)
Two	34%(24)	24%(28)	28%(20)	24%(28)
3 or more	25%(18)	7%(8)	13%(9)	6%(7)
Total	100%(71)	100%(118)	100%(71)	100%(118)

TABLE 5

DRUGS SELF-REPORTED TO HAVE PRODUCED ADVERSE REACTIONS,
SUBURBAN FOREST PRESERVE SAMPLE
(N=71)

Nature of Adverse Reaction	Drugs Said to Have Caused Adverse Reaction										
	Alc.	Pd.	Dust	H.	Am.	S-H	Cd.	Mh.	Solv.	Comb.	TOTAL
Physio-logical	29	9	8	7	5	4	3	2	2	2	71 56%
"Bad trip"	0	25	2	1	5	1	0	1	1	1	37 29%
Over-dose	0	1	2	4	2	2	1	0	0	0	12 9%
With-drawal	0	0	0	1	0	0	0	0	0	0	1 1%
other	0	0	1	4	1	0	0	0	0	0	6 5%
Total Number	29	35	13	13	13	11	4	3	3	3	127
% of Total	23%	28%	10%	10%	10%	9%	3%	2%	2%	2%	100%

Key to Abbreviations:

Alc.=Alcohol; Pd.=Psychedelics; Dust=Phencyclidine; H.=Heroin; Am.=Amphetamines; S-H=Sedative-Hypnotics; Cd.=Codaine; Mh.= Marihuana; Solv.=Solvents; Comb.=Combinations.

experiences of hallucinations, accounted for an additional 29 percent of the adverse reactions, and 68 percent of these were due to psychedelics such as LSD and MDA. Dust accounted for ten percent of the 127 adverse reactions; eight were physiological, two were "bad trips," and two were reported as "overdoses," a term which included from overdoses requiring emergency room treatment and less severe episodes of passing out.

Table six displays the total number of adverse reactions reported by subjects at Site two. Although the prevalence and frequency of alcohol use were similar at the two sites, alcohol accouuted for a considerably smaller percentage of adverse reactions at the urban site (four percent) compared to the suburban forest preserve (23 percent) . Psychedelics accounted for the greatest number of adverse reactions (31 percent), predominantly "bad trips." Amphetamines, sedative-hypnotics, and heroin were said to be responsible for a slightly greater percentage of the adverse reactions at Site two than Site one; the percentage of reactions due to dust was the same in both samples (ten percent at Site one and 12 percent at Site two). Dust was not mentioned in reactions said to be due to a combination of drugs. At both sites a greater number of "bad trips" was reported for psychedelics than for dust; but compared to psychedelics dust was said to be responsible for a greater percentage of adverse physiological reactions and those labeled by subjects as an "overdose."

Treatment of adverse reactions reported at Site two, displayed in table seven, was practically identical to the data from Site one. At Site two, 31 percent of the adverse reactions were treated by friends, 32 percent were treated at hospitals, 23 percent received no treatment, eight percent were treated by the subject himself, four percent were treated by parents, and two percent at drug rescue Services.

If we compare the type of drugs accounting for the adverse reaction and the nature of treatment reported at site two (see table seven), of all the drugs, psychedelics and dust had the greatest number of adverse reactions treated by friends (46 percent each). Twenty-three percent of the adverse reactions reported for dust, but nine percent of the adverse reactions reported for psychedelics, were treated in a hospital setting.

The data suggest that most reactions from dust and psychedelics are treated by friends, receive no treatment, or are managed by the individual himself. Hospitals appear to get subjects suffering from sedative-hypnotic and heroin overdoses, and overdoses and physiological reactions due to amphetamine abuse, more frequently than reactions said to be produced by other drugs, including dust.

Twenty percent of subjects at Site one and 34 percent at Site two had been treated at a hospital for a drug-related problem. The rank order of types of problems was the same among both samples: overdose, problems related to "heavy usage," adverse drug reactions, hepatitis, "to dry out," vehicle accidents due to drug intoxication.

TABLE 6

DRUGS SELF-REPORTED TO HAVE PRODUCED ADVERSE REACTIONS, URBAN SAMPLE
(N=118)

Nature of Adverse Reaction	Drugs Said to Have Caused Adverse Reaction										
	Alc.	Pd.	Dust	H.	Am.	S-H	Cd.	Mh.	Solv.	Comb.	TOTAL
Physio-logical	3	7	3	8	12	3	2	1	2	1	42 38%
"Bad trip"	0	27	6	0	3	0	0	2	0	2	40 37%
over-dose	1	0	4	7	1	5	0		0	5	23 21%
With-drawal	0	0	0	1	0	1	0	0	0	0	2 2%
Other	0	1	0	0	0	0	0	0	0	1	2 2%
Total Number	4	35	13	16	16	9	2	3	2	9	109
% of Total	4%	31%	12%	15%	15%	8%	2%	3%	2%	8%	100%

Key to Abbreviations:

Alc.=Alcohol; Pd.=Psychedelics; Dust=Phencyclidine; H.=Heroin; Am.=Amphetamines; S-H=Sedative-Hypnotics; Cd.=Codeine; Mh.=Marihuana; Solv.=Solvents; Comb.=Combinations.

TABLE 7

SELF-REPORTED TREATMENT FOR ADVERSE REACTIONS, URBAN SAMPLE
(N=118)

Drug Reported Producing Adverse Reaction — Reported Treatment

	None		Friends		Hospital		Self		Parents		Drug Prog.		Total	
	%	N	%	N	%	N	%	N	%	N	%	N	%	N
Alc.		(0)	75	(3)	25	(1)		(0)		(0)		(0)	4	(4)
Mh.	33	(1)		(0)	33	(1)	33	(1)		(0)		(0)	3	(3)
S-H	22	(2)	11	(1)	67	(6)		(0)		(0)		(0)	8	(9)
Am.	31	(5)	19	(3)	31	(5)	13	(2)		(0)	6	(1)	15	(16)
Dust	23	(3)	46	(6)	23	(3)		(0)	8	(1)		(0)	12	(13)
Pd.	26	(9)	46	(16)	9	(3)	11	(4)	6	(2)	3	(1)	32	(35)
H.	13	(2)	19	(3)	63	(10)	6	(1)		(0)		(0)	15	(16)
Oth.	23	(3)	15	(2)	46	(6)	8	(1)	8	(1)		(0)	12	(13)
Total	23	(25)	31	(34)	32	(35)	8	(9)	4	(4)	2	(2)		(109)

Key to Abbreviations:

Alc.=Alcohol; Mh.=Marihuana; S-H=Sedative-Hypnotics; Am.= Amphetamine; Dust=Phencyclidine; Pd.=Psychedlics; H.=Heroin; oth.=other drugs: Drug combinations and codeine, cocaine and glue.

Seven percent of Site one subjects and 23 percent of those at Site two had been hospitalized for psychiatric problems at least once. Approximately one-quarter of subjects at both sites considered themselves to have a "drug problem," but only ten percent wanted help with that problem. Approximately 20 percent of both samples had previously had some contact with a drug abuse treatment agency.

DISCUSSION

This study suggests that by utilizing a field team research model, public health agencies and drug treatment facilities could efficiently perform case finding and identify popular congregation areas for epidemiologic and ethnographic studies of drug use and as target areas for intervention. Incidence trends at these sites suggest that field intervention activity should be directed primarily toward reducing prevalence and frequency of use, case identification and early intervention with younger users prior to experimenting with intravenous use and opiates, and should place less emphasis on prevention approaches to reduce incidence of new cases experimenting with pharmaceuticals and psychedelic drugs (Hughes, Schaps, and Sanders 1973; Shick and Freedman 1975).

Regional congregation sites, such as we have described, attract a large population of heavy, multiple drug users, many of whom would not be included in studies conducted in schools, drug abuse treatment centers or industry. The large number of subjects neither employed nor attending school, the large number of grade school and high school droputs, and the numerous adolescent runaways identified suggest that field studies at such sites can contribute an added dimension to the study of multiple drug use. Furthermore, only about one-half of subjects out of school and unemployed could be identified through studies in hospital emergency rooms, psychiatric hospitals, and drug abuse treatment programs. Studies in the correctional system miss a large proportion of these youth. Although approximately 70 percent of both samples had been arrested at least once, approximately half of those arrested had been convicted.

The concentration of heavy drug users at such congregation sites suggests research investigating sequences of use (Kandel and Faust 1975; Gould et al. 1977) and precursors (Halikas and Rimmer 1974; Lettieri 1976) predictive of subjects at risk for adverse reactions or progression to dangerous patterns of multiple drug use, for example, intravenous experimentation. Perhaps regular attendance by adolescents at such sites itself may reflect high risk for adverse drug outcomes and other deviant behavior. The school and employment histories of subjects are in marked contrast to those of regular visitors to neighborhood locations previously studied (Shick, Dorus, and Hughes 1978) and suggest interaction between education and employment difficulties, drug using behavior, and alienation from mainstream youth more typical of other areas. The adverse outcomes implicit in all of this suqqest field studies to investigate causes, correlates, and consequences of social involvement in such settings.

Particular attention needs to be directed toward the composition and characteristics of groups, their requirements for membership, codes of loyalty and secrecy, status hierarchy, and territorial hangouts. The activities, preferences, common understandings, norms, and values need to be studied to increase our understanding of their relationship to drug use. Studies of how these youth chose to be certain types of teenagers, the labels they apply, and the behavior expectations of each role -- the deviations and the responses -- are part of our ongoing research. We need to know how newcomers learn about such areas, and how they are socialized into the group. The range, patterns, and characteristics of lifestyles in the community should be examined, and analysis should include examination of the appeals of illegal sources of support (or "hustles"), the socialization processes into such careers, and the relationship between these hustles and drug use. Studies should explore the popular folklore regarding specific drugs, methods of administration and the effects on patterns of use. They should describe how drug use is related to prestige -- or the loss of it -- and how drug use reflects the values and expectations of various groups, roles, and lifestyles.

These youth spend much of their time and activities with friends and acquaintances. Studies which concentrate only on drug use highlight drug centered activities to the exclusion of other behavior, often equally important in reinforcing or discouraging certain facets of drug use. Comprehensive field studies should place drug use in its broader social context by examining the patterns of collective activities (what they do together) and how much of their activities center around obtaining drugs and "getting high." For example, what sorts of activities first require getting high with drugs; when intoxicated, which activities are compatible and which are avoided? How do individuals and groups arrive at the decision to get high or to avoid taking drugs, and how is drug use related to risk-taking, recreation, and the sear& for novelty or constancy (Shick and Freedman 1975)?

Regular visitors to these sites were frequent users of a wide variety of drugs, often intravenously, but considering their frequent use, adverse reactions tended to be minimal. In fact, most adverse reactions were managed by the youth themselves and did not involve hospital contact, suggesting that studies of the extent and range of adverse reactions conducted at hospital treatment settings or identified through DAWN data may be biased toward the most severe reactions, include youth who are loners or least involved with drug using peer groups, or who are relative novices to the drug using scene.

Research into consequences and outcomes attempts to define a characteristic reaction, to understand a user's adaptation, and to assess the cost to the individual and society, as well as to delineate any neurochemical or tissue basis for a reaction, and/or operative personal, social or historical factors. Only rarely does research investigate such difficulties within the community, where a (so far) unknown number of users experience adverse consequences, yet define their difficulties in terms obviating -- in their minds anyway -- medical intervention: they remain contained, tolerated, or sheltered by their subculture.

These preliminary results suggest field studies investigating the specifics of what youth term "adverse reactions." For example, how do they define a "bad trip" or "overdose?" What do they mean when they say thats someone on the street has a "drug problem?" Do they apply the same or different criteria to themselves? Since so many adverse reactions are managed without treatment, by the individual himself or by his friends, what are the specifics of that management? How, in fact, do youth come to be treated at hospital emergency rooms; what are the selection factors? What drug problems are the "ticket of admission" for psychiatric hospitalization? How does a peer group decide that a reaction needs medical management?

The prevalence of intravenous experimentation among all age groups in these samples suggests a relative lack of social norms discouraging intravenous use and that patterns of chronic intravenous use my begin through acquaintances formed at such regional sites. How does the spread of intravenous experimentation occur? Do older, more experienced users initiate younger novices, or do friendship groups of novices obtain drugs and injection equipment from older users and try it for the first time among themselves? From a practical standpoint, it would seem that if a novice was determined to experiment with intravenous drug use, the presence of more experienced user might decrease the chance of an adverse reaction. S/he could impart the rituals and safety precautions born of experience without the novice's having to learn through trial and error. On the other hand, the older user might more quickly teach the novice to define the effects s/he experiences as pleasureful and reinforce further trials and, perhaps, habitual use (Becker 1967). If initial experimentation occurs among same-age friendship groups, how would peer pressure reinforce or discourage future trials? What portion of the friendship group would engage in future trials? The substance of the social norms about drug use and other behavior, the criteria drug using youth use to designate individuals with "drug problems," and the hierarchy of social roles in such settings are questions to be explored in future research.

We recognize the tentative nature of our findings. Our studies have focused on two regional (urban and suburban) congregation sites in Chicago. The similarities and differences between geographical and social organization of drug using groups and the patterns of drug availability and use in other communities with different ethnic and socioeconomic makeups should be investigated. Future comparative studies will define what segment of the total adolescent drug using population we have observed -- whether only the heaviest users hang out at such locations or whether infrequent users and nonusers have similiar congregation sites. At these areas we were able to obtain interview data on a sample only of the regular visitors.

Thus our findings do not necessarily reflect characteristics of other groups less frequently present.

The alleged epidemic of phencyclidine use is as yet poorly defined. Epidemics of drug interest and panic have occurred before, and societies have sought to regulate attitudes on the consumption of new or familiar substances; for example, the gin epidemic of 18th century Britain, the opium problem in the United States in the 1920's, the heroin epidemic among Chicago Negro youths and the Japanese epidemic of amphetamine use following World War II, and, of course, the "pot and acid" epidemic among white, middle class youths in the late 1960's (Shick and Freedman 1975; Shick, Smith, and Meyers 1970; Musto 1973).

We most not forget the potential influence of drug education program, of premature publication of research results, and naive, sensational reporting in the media. The public may have become supersaturated with the notion of drug abuse, and further input may serve only to reinforce interest in a deviant activity that, in reality, only small numbers engage in with seriously incapacitating outcomes. The treatment response must be directed toward those few, but what sort of treatment is effective remains a research issue. The prevention response has been hurriedly implemented without planning to research the needs of the receiver or the effectiveness of the output (Shick and Freedman 1971). The question of how and who should intervene needs careful planning and study and has numerous ethical, social, and legal implications.

Presently, phencyclidine is classified as Schedule III under the Controlled Substances Act of 1970. Interviews with fieldworkers and subjects suggest that in chicago rescheduling certain pharmaceutically manufactured substances, for example, Tiunal, Seconal, and Quaaludes, into Schedule II increased their cost, and initially at least, decreased their illicit availability. In Illinois, all Schedule II drugs require a triplicate prescription, and this may have been equally important in reducing supply (from pharmacies and pathological prescribers), a conclusion supported by field observations and informal interviews with users in the California area, where, for example, Quaaludes, which do not require triplicate prescriptions, appear to be more available (although similar in cost) than in Chicago.

Such rescheduling (into Schedule I or II) in the case of phencyclidine, which is supplied predominantly from illicit manufacture, will reduce supply less, if at all, my increase cost which is already substantial, and will have little effect on remission. It my encourage substitution reactions of potentially more dangerous drugs such as heroin.

Institution of tighter controls by National and State drug enforcement authorities, aimed at decreasing availability of drugs, ironically may have reinforced the establishment of an efficient illicit distribution system for nonopiate drugs (as well as increased their cost) and may have caused same users to substitute drugs, some of which, for example PCP, potentially may be more harmful. deAlaroon (1971) describes similar substitution reactions: the 19th century "ether epidemic" in Central Europe following the restriction of alcohol, the appearance of illegal "Chinese heroin" and the widespread intravenous barbiturate abuse in Britain after reducing the legal prescribing of heroin was reduced in 1969. His study of the effects in Britain of withdrawing injectable methedrine from the retail pharmacies reported that although the use of that drug declined, users transferred their preference to other drugs,and after two years one-third were still injecting (de Alaroon 1972). Lately, in the Chicago area, nonbarbiturate sedative-hypnotics which do not require triplicate prescriptions have become increasingly available as alternatives to barbiturates and methaquaalone. Amphetamine availability also dwindled subsequent to rescheduling, but large volumes of "uppers" resembling pharma ceuticals, but containing ephedrine and caffeine, and Schedule III and Schedule IV CNS stimulants replaced them.

Our research suggests that the nonopiate distribution system is more stable than previously envisioned and occurs in public places during warm weather, the residences of friends and dealers during the winter months, and at certain urban sites active throuhout the year (Shick and Wiebel 1978). In contrast to heroin addicts, visitors' regularity of attendance at these sites has little to do with physical dependence and seems to be determined more by the fact that adolescents hang out with drug using peers for recreational purposes. The demand (and supply) for drugs, which can be estimated from data on preference, prevalence, remission, and frequency of use,and their cost,appears to be great. Although the cost of these drugs is lower than for heroin, adolescents are not sufficiently wealthy to put-chase large quantities and may visit distribution sites more frequently than previously supposed. Whether this is due to problems of availability and cost or whether, as we suspect, it has more to do with the lifestyle and the influence of peer groups who supply drugs and initiate and reinforce certain types of drug use and their accompanying attitudes, are intriguing questions for field research studies.

ACKNOWLEDGMENTS

This research was supported by DHEW, National Institute on Drug Abuse Grant D A 01083. We wish to thank Mr. W. Wayne Wiebel, M.A., Mr. Norman Altman, Mr. Bruce Shaw, Mr. James Allen, and Mr.Gregory Shelton for their help in data collection and analysis.

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Chapter 8

Patterns of Phencyclidine Use

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INTRODUCTION

In recent years the use of phencyclidine (PCP) has been increasing. This increase has been accompanied by an evolution in conceptions about the motivation, patterns, and effects of phencyclidine use. These changing conceptions of PCP use have not necessarily reflected actual changes in use of the drug. In some cases they reflect the acquisition of new knowledge about the way the drug has in fact been used for a considerable period of time. This paper briefly examines some of the beliefs about PCP use and presents the results of an exploratory study of PCP users.

CHANGING CONCEPTIONS OF PHENYCLIDINE USE

When PCP use began to increase one of the first beliefs was that a person would not knowingly use the drug. Early sources of drug information (STASH, 1975) stated that PCP was not a drug of choice among young people. This information was found in drug information publications as late as 1976.

One probable reason for the hesitation to acknowledge PCP as a drug of choice was the drug's bad street reputation. This bad reputation was based on reports from San Francisco in the late 1960's on the negative effects of the drug. Another reason for the reluctance to acknowledge PCP as a drug of choice was the fact that many samples sent in for analysis to drug laboratories as THC or mescaline turned out to be PCP. The fact that PCP was often misrepresented as some other drug led many to believe that PCP was primarily sold that way. However, local reports from various areas indicated that PCP was a drug of choice for many young people during the early 1970's (Graeven 1977).

Once it was realized that there were PCP users who were aware of what they were taking, the next issue was whether or not phencyclidine use would spread. It was generally believed that PCP was a California drug and that it might be a fad limited to certain areas of that state. During the period from 1972 to 1976

PCP use had in fact spread to various parts of the country.

Reasons for the spread of PCP were that some users seemed to like the effects, the drug was easy to make, and the dosage could be regulated. Especially important for the spread of PCP was the change in mode of administration from pill to smoking (Graeven 1977). It appeared that in order for PCP to diffuse and increase in popularity as a drug of choice, less risky modes of administration such as smoking or snorting had to replace its use in pill form.

Recent survey data reported by the National Institute on Drug Abuse shows that PCP use has increased around the country (U.S. Journal of Drug and Alcohol Dependence, 1978). There now seems to be some agreement on the fact that many young people use PCP, and for some proportion of the users it is their drug of choice.

Currently the predaninant conception about PCP use, as presented in the mass media, is that PCP is an extremely dangerous drug. With the advent of PCP as a media event there seems a remarkable similarity to the drug information presented in the 1960's. At that time, there was a good deal of negative publicity, horror stories about users were published, and most often systematic research to support the statements being made was lacking.

The picture of phencyclidine use as a primarily negative experience is due in part to the fact that the spectrum of use has not been adequately examined. Most research reports have been based on people having problems with PCP. Early research on most street drugs, which is often based on persons found in treatment programs, is likely to overstate the frequency of negative effects as a result of using a drug, as well as overstating the importance of a lack of personal adjustment as a factor leading to its use (Graeven and Graeven, 1977). To present a valid picture of PCP use it is important that research look at the broad range of users.

METHOD

To examine the spectrum of PCP use an exploratory study was conducted. The goals of the study were to examine patterns of use, what people had heard about PCP, likes and dislikes about the drug and its perceived effects. A short questionnaire was administered to a group of 89 persons who had used PCP. Snowball sampling techniques were used, moving from known PCP users to their friends and acquaintances who had also used.

The majority of the sample was black (78 percent), with nine percent Mexican-American and twelve percent white. The majority came from the city of Oakland, California (68 percent), the remainder from Hayward and Fresno. Seventy-four percent of the sample was male and twenty-six percent was female. The median age was 20 with a range from 15 to 33.

USE PATTERNS

Results on total amount of PCP use shown in table 1 indicate that the largest group of users were those who used only once or twice (29 percent). At the other extreme, nine percent of the users had used more than one hundred times. Regarding frequency of use, almost half of the respondents seldom used PCP, with nine percent using it several times a day.

TABLE 1

PATTERNS OF PHENCYCLIDINE USE
(N=89)

Total Number of Times Used	%
1 or 2	29
3 to 8	21
9 to 30	28
31 to 100	13
100 or more	9
Frequency of Use	
Several times a day	9
3 to 5 times a week	14
1 to 2 times a week	14
Couple times a month	15
Seldan	48
Quantity used	
A few hits	36
½ joint	16
1 joint	26
2 joints	7
3 or more joints	15

All subjects reported that their most common mode of administration was smoking PCP joints. Diverse patterns were found for the amount usually used. As shown in Table 1, the modal amount used was a few hits from a joint. These data on use patterns indicate that for this population of users there was a large group of persons who seldom used the drug,but for the remaining persom there was a diversity in the total number of times used, frequency of use and quantity of PCP ordinarily used.

Analysis of the patterns of use by age showed that the age group 19 to 21 had the highest use. Twenty-six percent of those in the 19 to 21 year old groupused five times or more week, compared to eight percent in the 18 and under group and nine percent in the 22 to 30-year-old group. Comparing males and females, males were somewhat more likely than females to have high use. Twenty-three percent of the males used 31 times or more as compared to nine percent of the females.

DRUG OF CHOICE

Subjects were asked to choose which drug they preferred: alcohol, marihuana or phencyclidine. Eight percent preferred PCP, seventy-seven percent preferred marihuana, and fourteen percent preferred alcohol, Of those who used PCP frequently (3 or more times a week), a third preferred it. Marihuana was preferred by 43 percent of the high PCP users, and the remaining 24 percent of the high PCP users preferred alcohol. None of the subjects with lower use patterns preferred PCP.

HEARD ABOUT PCP

Respondents were asked an open ended question on what they had heard about PCP. Fifty-three percent had heard that people liked PCP; one third had heard that PCP was physically bad for a person. The main negative physical effect mentioned was that PCP could kill brain cells. The third most frequent response was that most people couldn't handle PCP (14 percent). Inability to handle the effects of PCP was indicated by responses such as "people would act crazy" or "people get into trouble on PCP."

Comparing patterns of use by what people had heard about PCP showed that the more frequently PCP was used the more likely the respondent reported that s/he had heard that people liked the drug. Forty percent of the people who seldom used PCP had heard that people liked it, as compared to 54 percent of those who used it a couple of times a month and 75 percent of those used one or more times a week.

LIKE MOST ABOUT PCP

In response to an open ended question on what was liked most about PCP, the majority of the respondents (58 percent) said the high they get when they use it. Twenty-nine percent said there was nothing they liked about the drug, and twelve percent liked the way they acted when they were on PCP. Comparing use patterns by what they liked about the drug,the group with the lowest use pattern,as would be expected, was most likely to mention that there was nothing they liked about the drug.

DISLIKE MOST ABOUT PCP

In response to an open ended question on what they disliked about the drug, nearly two-thirds (63 percent) of the respondents mentioned the lack of control of themselves when they weres on PCP, e.g., "I can't control my body," or, "I can't control my thoughts." About one-third (37 percent) stated that there was nothing they disliked about the drug.

Those persons who used PCP most often were least likely to mention lack of control as a problem and most likely to say there was nothing they disliked about the drug. Thirty-six percent of those who used PCP three or more times a week mentioned lack of control as what they disliked about the drug as compared to 73 percent of those who used the drug two or less times a week.

PERCEIVED EFFECTS OF PCP

Questions were also asked regarding whether subjects never, always, or sometimes had each of four experiences when they used PCP: felt good, forgot their worries, liked to party, and had mood changes. Field work suggested that PCP users varied in that some persons liked to move around and dance while on a PCP (party), while others didn't. The responses to these questions are shown below in table 2. For each of the four experiences there was no overwhelming agrees-tent on any one of the response categories. Modal responses showed, however, that respondents were not likely to forget worries or feel good about themselves while using PCP, and were somewhat likely to party and have mood changes when using.

TABLE 2

PERCEIVED EFFECTS OF PCP
(N=89)

Behavior	% Never	% Sometimes	% Always
Forget worries	48	33	19
Feel good about self	38	37	25
Like to party	35	42	23
Mood changes	23	38	39

There was no relationship between patterns of PCP use and mood changes, forgetting worries; and feeling good about oneself. For 'partying," there was a slight relationship with the amount of drug used. Thirty-six percent of those who used PCP three times a week or more always partied on PCP as compared to 17 percent of those who used two or fewer times a week.

LACK OF CONTROL AND PERCEIVED EFFECTS

Comparing the perceptions of those who mentioned lack of control as one of the adverse effects of PCP with the group that said they had no problems with the drug revealed some interesting results. While there were no differences between groups on forgetting worries or mood changes, there were marked differences for "feeling good" and "partying." For those who disliked the lack of control, only three percent always felt good when using PCP as compared to forty-six percent of those who did not mention lack of control. For partying, eight percent of the lack of control group always partied when using PCP, as compared to forty-one percent of those in the other group.

The difference found in the perceived effects of PCP for those who did and did not dislike the lack of control, poins to an interesting dimension of an individual's reaction to PCP use. reaction to loss of control and whether or not a person experiences the loss of control seems to have consequences for how a person behaves under the influence of PCP.

SUMMARY

Use of phencyclidine is a diverse phenomenon with wide variations in both the amount taken and the frequency of use.There is a large group of persons who have tried PCP once or twice and discontinued using. One of the key distinctions pointed out by this exploratory study relates to the feelings of control persons have over the effects of the drug.The PCP user who is not bothered by the lack of control is more likely to feel good and party with others when using and is more likely to have high use patterns. Feelings of control over the effects of PCP indicate an important individual difference in understanding reactions to PCP use and further research should systematically examine this phenomenon.

There has been a discrepancy between our conceptions of PCP use and the actual patterns of use found in the United States. It appears that at this time most persons in the drug abuse field are willing to accept the fact that PCP is a drug of choice among young people and that some as yet unspecified proportion of users is able to use PCP and avoid major problems. While there remains much speculation about the motivation for use and the effects of such use,it would appear that we are ready to engage in research which systematically looks at the spectrum of users.

ACKNOWLEDGMENTS

I would like to thank Fredonia Honable, Beulah Brewster,and James M. Washington for their assistance in the collection and analysis of the data.

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Chapter 9

The Psychiatric Aspects of Chronic Phencyclidine Use: A Study of Chronic PCP Users

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INTRODUCTION

Phencyclidine (PCP) first appeared on the "streets" as an abused drug in 1967, two years after human clinical investigations of its potent analgesic and anesthetic effects were discontinued because of its severe behavioral side effects (Reed and Kane 1972). Since that time illicit synthesis and abuse of PCP have increased under the guise of various street names, such as TIC, TAC, THC, angel dust, dust, dummy dust, rocket fuel, hog, sheets? crystal and crystal joints (Fauman et al. 1976). Investigation of PCP's psychotomimetic effects were conducted in the early 1960's, coincident with early clinical trials of the drug (Davies and Beech 1960; Bakker and Amini 1961: Luby et al. 1962). In the early 1970's the first reports of adverse medical and behavioral side effects, including severe longterm psychotic episodes from street PCP began to appear (Reed and Kane 1972; Stein 1973; Rainey and Crowder 1974; Burns et al. 1975; Eastman and Cohen 1975; Fauman et al. 1975; Luisada and Reddick 1975; Tong et al. 1975; Liden, Lovejoy, and Costello 1975). Since that time abuse of PCP has increased and has spread to all parts of the country. Several recent papers have alerted physicians to the varied medical and psychiatric presentations of PCP ingestion at low doses and in cases of overdose (Fauman et al. 1976; Luisada and Brown 1976; Bolter et al. 1976; Burns and Lerner 1976; Cohen 1977; Dupont 1977; Aronow and Done 1978). Quantification of amounts of ingested phencyclidine is often difficult because many street preparations are mixtures of phencyclidine and other drugs, patients may come to medical attention at varying times after using the drug, and many medical centers do not have the necessary laboratory facilities to test for phencyclidine (Lundberg, Gupta, and Montgomery 1976; Aronow and Done 1978).

Recent concern has also been directed to the effects of chronic abuse of phencyclidine (Burns and Lerner 1978). The presence of chronic abuse implies that the phencyclidine experience is not always as dangerous or undesirable as recent medical reports have suggested. This paper reports the results of a pilot psychiatric study of a sample of chronic phencyclidine abusers whose length of use of this drug ranged from ten months to nine years. Specifically, we have attempted to investigate the manner of phencyclidine use, its psychological and interpersonal effects, bad reactions from phencyclidine, and the sequelae of its abuse. We have also tried to determine why its use is so widespread despite its potentially dangerous side effects, the attitudes of users toward PCP, and its effects on their lives. Finally, we hope to point out the direction of further studies in this area, related to the psychiatric and neuropsychological effects of chronic phencyclidine abuse.

A STUDY OF CHRONIC PHENCYCLIDINE (PCP) USERS

Phencyclidine Study Population

Crossroads is a residential therapeutic community for the treatment of polydrug abusers between thirteen and twenty two years of age.[1] It is operated by the Illinois Dangerous Drugs Rehabilitation Systems (IDDRS), a private not for profit corporation. The residential program maintains a census of 35-40 clients. The census at the time of the study was 8 women and 28 men. Thirty two of the 36 clients had used phencyclidine in the past and 29 clients (81.1 percent) had used phencyclidine for 10 months or longer (average 3.6 years ± 1.8 years). Twenty five clients who were chronic phencyclidine users consented to be interviewed.

Phencyclidine Study Questionnaire

The study questionnaire consisted of 73 questions about the user's family, schooling, psychiatric history, knowledge about phencyclidine, and use of phencyclidine. The study was explained to the client and s/he was told that participation was totally voluntary. Confidentiality was maintained by recording only the first name and last initial on the first page of the eleven page questionnaire. The pages were then nunber coded and separated for analysis. The questions were administered to the phencyclidine user in a 45 minute interview with one of the senior authors.

PCP Users: Demographic Data, Personal and Family History

Tables 1 and 2 present demographic data and some personal and family historical data for the 25 users in the study. The five women reported considerably less average weekly spending money than the men. Three of the five reported that their boyfriends supplied them with phencyclidine so they did not need to buy the drug. A substantial number of parents of PCP users were also reported to use some form of drugs regularly. Seven PCP users had fathers who were alcoholic and two of these seven also had alcoholic mothers. Alcohol was the cause of death of one of these mothers. Three other mothers and two other fathers routinely used depressants, mainly diazepam. Two other mothers and one other father routinely used pain medication. Two PCP users reported that their mothers had been hospitalized for psychiatric problems

TABLE 1

PCP USERS: DEMOGRAPHIC DATA

SEX	REACE WHITE	BLACK	AGE	YRS OF SCHOOL	# OF SIBS	WEEKLY SPENDING MONEY
MALE	19	1	19.0 ± 1.9*	10.6 ± 1.2	4.0 ± 3.0	$238 ± 176
FEMALE	5	0	17.8 ± 2.5	10.6 ± 0.9	1.6 ± 1.1	$76 ± 31
AVERAGE			18.8 ± 2.0	10.6 ± 1.1	3.2 ± 2.2	$205 ± 170

*Standard Deviation

TABLE 2

PCP USERS: DEMOGRAPHIC, PERSONAL AND FAMILY HISTORY

HISTORICAL INFORMATION	% OF USERS WHO REPORT		
	MALE	FEMALE	AVERAGE
Parents separated or divorced	25	20	24
Mother used drugs*	30	40	32
Father used drugs*	40	60	44
User was only child	5	20	8
User was eldest child	40	40	40
Previous family psychiatric problems	30	80	40
Previous user psychiatric problems	40	40	40
Previous user suicide attempt	20	40	24
Previous user OD from any drug	35	40	36
Users who report that drugs interfered with school	60	60	60

Sample size: 20 Male, 5 Female

* Drugs include: Downers, Marihuana, Alcohol, Heroin, Pain Medications

and one reported that a sister had been hospitalized for drug problems. The remaining family psychiatric problems included alcoholism, hyperactive siblings, marital problems and nonspecific psychiatric problems. Ten phencyclidine users reported previous psychiatric problems, often related to drug abuse. Nine users reported drug overdoses and four reported more than one overdose. Most users who attempted suicide did so by taking drug overdoses. Others were quick to point out that their overdoses were not conscious suicide attempts, but were instead accidents.

Many phencyclidine users reported that drugs interfered with their schoolwork. Some were too "high" or "spacey" to be able to get up in time for school or concentrate on their schoolwork. For others, drug use, family and other interpersonal problems together led them to leave school and often, their homes.

PCP Users: Drugs Used and Favorite Drugs

Table 3 presents the drugs used and favorite drugs of participants in the study. Phencyclidine was reported as the favorite drug for 56 percent of the users, because of its availability, low cost, but mostly because of the effects they obtained from it. Eighty eight percent (22) of the phencyclidine users had used LSD and 84 percent (21) had used it heavily, more than 24 times. All 88 percent reported that the experience obtained from LSD was different from phencyclidine. Most felt that LSD has more of a hallucinogenic effect, with colors and images, while phencyclidine produced more of a "body high" with sensory distortions, but not vivid visual hallucinations.

PCP Users' Beliefs About the Dangers of PCP

Ninety six percent (24) of users had heard that phencyclidine is a dangerous drug, and 88 percent (22) believed that it was dangerous at the time of the study. Fifty two percent (13) had heard this from friends, 32 percent (8) from drug counselors, 16 percent (4) from family, 24 percent (6) from reading, and 12 percent (3) decided phencyclidine was dangerous from personal experience. Clients reported they had heard that phencyclidine contained impurities, caused coma and death, killed "brain cells," makes you "rowdy" and "stupid," causes brain damage and psychosis, "burns you out," causes cancer and liver damage, and can cause convulsions. Many, if not most, of the phencyclidine users we spoke with had heard and believed that phencyclidine was dangerous before they entered the treatment program, but this apparently did not stop them from using it for as long as nine years. Some users reported that they could not stop using phencyclidine. One 20 year old user, who was asked to leave the program after six weeks because of his behavior, immediately used phencyclidine intravenously the day he left, even though he believed it was dangerous. He was later readmitted to the program.

TABLE 3

PCP USERS: DRUGS USED AND FAVORITE DRUG(S)

DRUG USED	% WHO USED DRUG	% WHO REPORTED DRUG AS* THEIR FAVORITE DRUG
Uppers (Stimulants)	72	4
Downers (Depressants)	92	20
Marihuana	52	0
Alcohol	36	0
Glue	12	0
Cocaine	80	12
Phencyclidine	100	56
LSD, Mescaline	88	16
Heroin	40	4
Other Opiate	20	0

Sample size: 20 Male, 5 Female

*4 Male users reported 2 favorite drugs and 1 Male user reported no favorite drug

Availability and Use of PCP

All of the users questioned stated that phencyclidine was easy to obtain. Many laughed at the question and described going into the parks or along the shores of Lake Michigan, and hearing young dealers advertising their wares by yelling "Get your angel dust, acid and coke here." Another user described how student dealers regularly used specific stalls in the school bathrooms to sell phencyclidine and other drugs. Still others described comparison shopping for phencyclidine on the street corner, asking three dealers to show how much phencyclidine they would sell for ten dollars. Most users agreed that the availability of phencyclidine was independent of the time of year.

Phencyclidine was purchased in "dime" amounts or grams. A "dime" cost ten dollars and contained an unspecified amount of drug, usually arrived at by bargaining between user and dealer. A gram of phencyclidine sold for approximately sixty dollars and contained between 15 and 22 "dimes." Users also referred to two, three, and five cents worth of phencyclidine, meaning subdivisions of a "dime" into amounts of PCP worth two, three, and five dollars.

Sixty eight percent (17) were introduced to phencyclidine by friends and 16 percent (4) were started by dealers. Users reported first hearing about phencyclidine at an average age of 13.4 (±1.6) years and first using PCP at an average age of 14.2 (±1.5). Fifty six percent (14) indicated that they used phencyclidine continuously from the time they started until entering the treatment program. Others stopped when they moved out of the country, could no longer afford PCP, were going with women who asked them to stop, entered drug treatment programs, or became concerned about the side effects. Sixty percent (15) of users felt that phencyclidine was more special than other drugs, either because of its availability and low price, or because of the effects it produced. Finally, users estimated that 97 percent of their friends used drugs, and 75 percent used phencyclidine.

Table 4 shows the frequency of phencyclidine use among the study population. The first three columns in figure 4 report the user's estimate of the period of his/her heaviest use, including the number of times per day, number of days per week PCP was used, and the number of months this heavy use continued. The last column reports the average total number of years of PCP use. The months of heaviest use vary the most, with a range of 0.5 to 60 months for men, and 2 to 12 months for women. Similar high estimates of the frequency and duration of PCP use were obtained independent of the senior authors by one of the staff nurses.

It is possible that the reporting of these high levels of PCP use, as well as the frequent reporting of PCP as the drug of choice, was influenced by the fact that our subjects knew we were interested in PCP use. We asked about the use of one other drug, LSD, in some detail. As mentioned earlier, 21 users reported they had

TABLE 4

PCP USERS: PERIOD OF HEAVIEST PCP USE AND TOTAL YEARS OF PCP USE

	PERIOD OF HEAVIEST USE OF PCP			
	TIMES/DAY	DAYS/WEEK	DURATION IN MONTHS	TOTAL YEARS OF PCP USE
MALE n=19	2.5 ± 1.5* (1-5)¶	5.8 ± 1.9 (2-7)	16.6 ± 19.4 (0.5-60)	4.4 ± 1.7 (1-9)
FEMALE n=5	2.2 ± 0.8 (1-3)	6.0 ± 1.4 (4-7)	6.2 ± 3.9 (2-12)	3.6 ± 1.5 (2-5)
AVERAGE n=24	2.5 ± 1.4	5.8 ± 1.8	14.4 ± 17.8	4.2 ± 1.7

* Standard Deviation
¶ Range of Values

used LSD heavily. For the nine who gave more specific data about their use of LSD, the average frequency was 3.2 (±2.8) times per week, for an average of 18.6 (±16.0) months. The fact that they reported a high incidence of LSD use suggests a different bias, namely that our study sample probably consisted of heavy users of multiple drugs.

PCP Users: Knowledge of Bad Reactions to PCP in Others

Eighty eight percent (22) of PCP users in the study reported incidents of friends having bad reactions to phencyclidine. One incident involved a friend who fell into the water and had to be rescued because he couldn't move or swim after taking phencyclidine. Two others reported incidents of friends becoming belligerent and starting fights, and four users reported bad reactions in which friends could not move, or lost control of the car they were driving, and hit other cars. Some became concerned that they were going to die, while others feared that they would never "come down." Fifteen users had heard of or knew at least one person who had a prolonged bad reaction to PCP, with some requiring medical attention. Six of these were not specific about the length or severity. Five reported the reaction lasting 3 to 5 days, two reported bad reactions lasting two weeks, and two persisted for two months or more. Some prolonged "bad trips" included psychotic delusion, severe paranoia and attempts at self-mutilation.

The Phencyclidine Experience

The descriptions phencyclidine users gave of their first experience using PCP varied considerably. One woman and 11 men described the experience in very positive terms: fantastic, "mind blowing," an intense high, or a happy experience. Four women and six men found the experience neutral or mildly unpleasant. One of these reported he had taken an overdose on "five cents worth" of PCP and became numb. A second fell into the water, thought he would drown, and barely pulled himself out of the water before he became unconscious for three hours. The third reported that he started with a "dime" of PCP and then added more, until he became stuporous for five days, periodically awakening with hallucinations. A number of users described the experience as one of feeling "light," as if they were walking on air or on clouds. Others described feeling numb, pleasantly dissociated from their bodies, unable to move, calm or "mellowed out," as if they had taken a tranquilizer, or feeling stimulated and excited. A few had a feeling that everything was in slow motion. One male user described feeling rowdy.

The usual phencyclidine experience varied considerably from user to user, and was also distinctly different from the first experience. None of the women and seven of the men reported the usual PCP experience as being positive. They described feeling high, calm, "mellow," or euphoric. Three women and eight men found the experience to be unpleasant. They described feeling numb, unable to understand people, paranoid, scared, exhausted, moody, unable to move, and generally isolated from the environment. Three men described feeling “rowdy” or violent. The usual PCP experience was generally described as more dysphoric than the first experience. Some users began to feel increasingly moody or chronically numb and slowed. The same feelings which were described positively for the first experience began to be described in a negative sense as use continued.

Phencyclidine users were asked how their friends described the user’s behavior when s/he was taking PCP. The female users were described as “cool,” fairly normal, calm, or “spacey.” Eight of the males were described as becoming irritable, rowdy, or starting fights while taking phencyclidine. One reported that he threw a 55 gallon aquarium off a stand and burned a car while under the influence of PCP. Two others were described as acting erratic, from being calm to attacking others for no reason.

Phencyclidine users were also asked to describe the behavior of their friends when they used PCP. Friends were most commonly described as acting “goofy" or like robots, not knowing what they were doing or saying, bumping into objects, acting stupid, and talking slowly with slurred speech. Nine users described friends as acting rowdy, irritable, or picking fights on phencyclidine.

Fifty two percent (13) of users described their feeling immediately before using PCP as scared, insecure, depressed, lonely, bored, “uptight,” or misunderstood. Others described a need to be high or the feeling of needing to “get away from things.” Forty four percent (11) described feeling excited, eager, or “anticipating” using PCP. After using PCP, some felt sad that they were right back to the same problems they started with, while others felt that they now had no worries. Many felt tired or worn out, and some felt regret that they had used PCP again.

Table 5 shows information on the manner of use and experience of phencyclidine. The predominant mode of use is “snorting,” inhaling phencyclidine in powder form. Next most common is intravenous injection of PCP, although only one user employed intravenous injection as the sole method of use. Three subjects only snorted PCP; the remaining users employed combinations of modes. Only one reported usually taking PCP when alone. Others usually took PCP with at least one additional person present.

Seventy six percent (19) of users reported having “bad trips” on phencyclidine. The most commonly described severe symptoms included numbness and loss of motor control, or paralysis, confusion, sensory distortions and loss of consciousness. A few reported cramps, nausea and emesis. Two users had auditory hallucinations. two became violent, and two others became very paranoid during the experience. Others described loss of

TABLE 5

PCP USERS: THE PCP EXPERIENCE

	% OF USERS WHO REPORT		
	MALE	FEMALE	AVERAGE
Method of PCP Use			
Intravenous	50	80	56
Smoked	50	60	52
Snorted	95	100	96
Eaten	45	60	48
How Used			
Alone	50	40	48
Another Person	65	80	68
Group	70	60	68
One Bad Trip	75	80	76
Continued to Use PCP After Bad Trip	70	80	72
More than One Bad Trip	55	20	48
Memory Loss During PCP Use	90	100	92
Paranoia During PCP Use	60	40	56
Need or Crave PCP	75	40	68
Physical Withdrawal	25	0	20
Difficulty with Directions on PCP	50	0	40
Flashbacks	35	0	28

judgement and memory which sometimes involved them in accidents. One reported trying to cross a busy street, looking one way and then the other for cars, but immediately forgetting what he had seen when he turned his head. He finally decided to step into the street and ran into a car. Only three users reported being taken to a hospital during a "bad trip." Two of these were discharged within a day, and the third remained on a psychiatric ward for two weeks. In the entire group of phencyclidine users, this was the only report of a personal experience of a prolonged psychotic reaction, including auditory and visual hallucinations and violent behavior. Most users who had bad trips experienced them alone, or waited them out with friends, rather than seek medical attention. One woman reported that she would “check my body out part by part” when she was experiencing the numbness and paralysis of a bad trip. Generally, the experiences that phencyclidine users reported for “bad trips” were similar to some of the dysphoric sensations described during their usual PCP experience, with the difference that the ‘bad trip” sensations were far more intense and upsetting to them.

Despite the fact that 76 percent (19) of PCP users had one “bad trip” and 48 percent (12) had more than one, 72 percent (19) continued to use the drug. Six users reported that they needed phencyclidine or liked it enough to continue. Five rationalized the bad trip as being caused by circumstances, impure drug, too much drug, or else felt that they had not had a bad enough “bad trip” to deter them. Others reported that they used phencyclidine again because it was freely available when no other drug could be obtained.

Sixty eight percent (17) of PCP users stated that they felt a need or craving for phencyclidine. Only 20 percent (5) reported physical symptoms of withdrawal, describing these as nervousness, upset stomach, “the shakes,” and “cold sweats.” One user stated that PCP satisfied his craving for heroin. Another described how his need for PCP caused him to carry some with him wherever he went.

Many users reported a gradual change in their mood while using PCP. Thirty two percent (8) indicated that their mood had become more angry, irritable, or violent during the time they were using phencyclidine regularly. Others reported becoming more antisocial, depressed, lonely, or isolated from people. Sixteen percent (4) felt that using phencyclidine had produced positive changes in their personalities. They described feeling more comfortable, socially easy going, hard working, and more “masculine.” The majority of users felt that they had become more selfish. Many reported losing their friends because of the changes in their personalities.

We assessed cognitive functioning only superficially, by asking users whether they had problems with memory, finding directions, or making change (figure 5). Ninety two percent (23) indicated substantial memory loss during the period of time they took PCP.

Thirty six percent (9) felt that their memory had improved within two to three weeks after stopping phencyclidine, in the treatment program. Forty percent (10) indicated difficulty figuring out directions while on PCP. One user reported getting lost three blocks from his home.

“Flashbacks” are usually described as the reappearance of a drug effect when the drug has not recently been used. Twenty eight percent (7) of PCP users experienced one or more flashbacks. Sixteen percent (4) of these occurred when the individual smoked marihuana after the PCP “high” had worn off. Finally, most users reported the development of tolerance to PCP, requiring higher doses to achieve a high. They usually started with two or three “cents” worth of PCP, which made them quite high. Eventually, most subjects were using one to two “dimes” at a time, and often up to a gram of PCP in a day.

DISCUSSION

Chronic Phencyclidinc Abuse

Recent observations have indicated that the use of phencyclidine, and more specifically, its role as drug of choice, has increased markedly in the last year or two (DuPont 1977; Taylor 1978). Our study corroborates these observations, finding an extremely high prevalence of PCP use and choice of PCP as the preferred drug for a sample of chronic polydrug users. Considering the frequency and combined length of PCP use (a total of 105 years) in the study sample, most users titrated or adjusted their consumption well enough to prevent more than rare "bad trips.” Furthermore, since our study indicates that relatively few “bad trips” are brought to medical attention, estimates of PCP use based on hospital statistics may be very low.

The initial and early experience with phencyclidine is usually reported as a pleasurable or carefree “high” or numbness. The experience is novel, short lived, and appears to provide an escape from anxieties, depression, or external pressure. These early experiences are almost always with low doses of the drug: two, three, or five “cents.” Gradually, users become tolerant to the effects of low doses of PCP, take larger amounts more frequently, and begin to relate increasingly dysphoric experiences on phencyclidine. The initial enjoyable sense of being “high,” numb, isolated, and unable to move becomes more intense and sometimes distinctly unpleasant. Although some users continue to enjoy their experiences with phencyclidine, for the most part the comments become more critical of the drug. It was initially difficult for us to understand why many of those we interviewed continued to use PCP despite these unpleasant experiences. We now believe that many users felt trapped by the drug. They remembered their initial good experiences, and probably still had some enjoyable “highs” during their period of chronic use. In addition, the drug began to assume magical properties for some users, who reported that they carried PCP with them almost like an amulet.

Others couldn't explain why they continued, except to say that they needed to use it, or that it was cheap and available. Nevertheless, it would be a mistake to claim that availability was the major reason for the popularity of PCP. We feel that its popularity is a combination of the effects it produces and its availability, with the former perhaps the more significant.

Three types of adverse phencyclidine reactions were reported as "bad trips." Episodes of cramps, nausea, and emesis after taking PCP may be due to impurities in the drug caused by incomplete synthesis (Reed and Kane 1972). Prolonged psychotic reactions of more than two weeks duration appear rare, and will be discussed in more detail below. The majority of reported "bad trips," consisting of severe numbness, isolation, paralysis, confusion, transient psychotic behavior, hallucinations, stupor or coma, appear to be extreme examples of the dysphoric sensations described for the usual PCP experience. We feel that these "bad trips" are probably due to the periodic use of very high amounts of phencyclidine, especially in individuals who are already using large amounts. This would suggest a continuity between early pleasurable "highs" with low doses of PCP, and later dysphoric feelings with larger doses. In essence, phencyclidine produces an organic brain disorder (Fauman and Fauman 1977; Fauman 1977). In low doses, the organic brain disorder is mild and often pleasurable. As users become tolerant to phencyclidine and use larger doses, they may develop a chronic organic brain disorder (Cohen 1977). Reports of chronic memory loss support this conclusion. Periodic additional excessive amounts of phencyclidine may produce toxic psychotic episodes or intense isolation and loss of body control which is very frightening to users and often stimulates fantasies of dying or remaining permanently dysphoric. Such "bad trips" end as the phencyclidine is metabolized and excreted. It is also possible that the interpersonal and social circumstances contribute to the chemical effect of a large dose of the drug to produce the "bad trip."

This study also suggests that there may be significant personality changes associated with chronic phencyclidine use. Many chronic users reported the same increase in irritability, violence and rowdiness that has been described for the phencyclidine-induced psychosis (Luisada and Reddick 1975). Increased irritability and belligerence is a common finding in patients with chronic organic brain disorders (Fauman and Fauman 1977). Our study also suggests that many phencyclidine users have difficulty tolerating anxiety and depression or common stresses of daily life. They use phencyclidine as a means of escaping from these feelings, only to have them return after the "high" passes.

The Prolonged Phencyclidine Psychosis

Before we undertook this study, it was our impression that phencyclidine regularly caused prolonged psychotic reactions (Fauman et al. 1975). These reactions typically are present as bizarre behavior, with confusion and agitation: the patient may be mute and staring, and unresponsive to painful stimuli. There is usually a history of a sleep disturbance if the patient presents some time after the drug exposure, and evidence of cerebellar dysfunction, including nystagmus, ataxia, and dysarthria, if the exposure has been fairly recent. In some cases, the patient is also violent or aggressive, particularly when s/he feels threatened. In nearly all subjects there is a striking degree of fearfulness. The patient may be diagnosed as schizophrenic if the history of drug use has not been obtained. These symptoms persist for several days to two weeks before beginning to remit, and may take an additional four weeks to clear.

As an increasing number and range of reactions came to our attention from our emergency department and in consultation with other hospitals, most of which did not fit our description of the psychosis we had seen initially, it began to appear that the reactions were dose dependent. Eventually, as we learned of the widespread availability and popularity of this drug, we speculated that only a small number of people using the drug were susceptible to the prolonged psychosis (Faunan et al. 1976). In our review of prolonged psychoses related to other drugs, it appeared that this was also true for the severe psychiatric morbidity that occurred rarely with cannabis, LSD, and amphetamines. Most authors suggested that there was an idiosyncratic propensity in those people who developed psychoses. This corresponds with the data from early work with phencyclidine. Normal volunteers experienced a brief psychotic reaction that was dose related (Davies and Beech 1960; Bakker and Amini 1961), but schizophrenics had prolonged exacerbations of illness (Luby et al. 1962). Recent reports also support this, as Luisada noted that one quarter of his series were readmitted with recurrent psychotic illness, with no additional exposure to phencyclidine, after an initial PCP-induced psychosis (Luisada and Reddick 1975). He felt that these patients represented a part of a continuum between normals and schizophrenics.

It is clear from our study that for some, phencyclidine use is not merely recreational, weekend, or experimental, but has become a regular and prolonged habit. With an accumulated total of 105 years of use in our study sample of 25 users, the appearance of only one prolonged psychosis similar to those described by Luisada and our previous observations suggests that PCP cannot be the sole cause of the prolonged psychosis. It appears that the prolonged phencyclidine psychosis may be the most dramatic effect of the drug and the one most likely to come to medical attention. Nonetheless, it is rare, and not the most devastating effect of this drug.

The Direction of Future Investigation and Treatment

It should be realized that there are two distinct aspects of phencyclidine abuse. The first is the special problem of the drug phencyclidine, its use, and its dangerous sequelae. Equally important is the type of personality problem which leads individuals to use drugs like phencyclidine. It is important not to overlook the latter problem, because it is this one which will remain long after phencyclidine has disappeared. Phencyclidine is popular because of the effect it produces as well as its availability and low cost. Nevertheless, there are now, and will be in the future, other drugs which have similar effects and may well become as much of a problem as phencyclidine is at present.

We feel that there are three major areas for future work related to polydrug abuse, and specifically, phencyclidine abuse. First, the behavioral and neuropsychiatric effects of chronic phencyclidine abuse must be studied and methods of treatment devised. This expressly includes an assessment of the potential acute and chronic organic brain disorder caused by phencyclidine. In addition, the serious effects of phencyclidine should continue to be publicized. Second, there should be more investigation and attempts at treatment of the underlying personality problem that leads to abuse of drugs like phencyclidine. Finally, there should be an active monitoring of the polydrug abuse population for early detection of new drugs with a potential for abuse. Hospital emergency departments should be alerted to these drugs, and methods of treatment for the side effects and over-dosage developed and quickly disseminated to treatment centers.

FOOTNOTE

1. This study was conducted in December 1977 - January 1978, at the Crossroads Youth Program, 7400 West 183rd Street, Tinley Park, Illinois 60477.

ACKNOWLEDGMENTS

The authors would like to thank Peter J. Bokos, Executive Director, Illinois Dangerous Drugs Rehabilitative Systems (IDDRS); Michael Taylor, Director of Crossroads, and staff members .Jane Early, R.N., and Pat Sohanski., R.N. , for their generous assistance in the completion of this project.

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Chapter 10

Phenomenological Aspects of Phencyclidine Abuse Among Ethnic Groups in Hawaii

Anthony J. Marsella, Ph.D., and Russell D. Hicks, M.D.

INTRODUCTION

The fact that phencyclidine, a drug originally developed in the early 1950's by Parke, Davis and Company for use as a nonnarcotic intravenous anesthetic agent, could emerge as a popular recreational and quasi-therapeutic drug among our nation's youth, raises a number of interesting questions about the nature of the phenomenological experience associated with phencyclidine use. The purpose of the present paper is to examine some of these questions through a review of our clinical experiences with phencyclidine users and to offer some speculations about the possible reasons why young people begin and continue to use phencyclidine.

The Hawaii Job Corps

This discussion of phencyclidine is based on our experiences as Director of Mental Health Services and Director of Medical Services for the Hawaii Job Corps, a Federally-funded residential program to provide educational and vocational training for high school dropouts between the ages of 16 and 21. It also provides medical, psychological, and recreational services. The program generally requires from 18 to 24 months to canplete. The Hawaii Job corps in Honolulu has about 220 enrollees (55 females, 165 males) who reside in four dormitories. Because of disciplinary and personal adjustment problems, the turnover is high. Nevertheless, the program completion rate runs around 40 percent.

The enrollees consist mainly of youth of mixed Hawaiian racial ancestry ("locals") who cone from the rural areas of Oahu. The second largest ethnocultural group represented consists of Micro nesian youth. They are followed in number by Guamanians, Samoans, Caucasians (mainly armed service dependents), Filipinos, and a few Korean and Vietnamese immigrants. All of the enrollees are from the lower sociceconomic class strata and many have personal histories of delinquency and school maladjustment. Divorce, child abuse, and parental rejection are present in many life histories. Polydrug abuse and alcohol abuse occur in 80-90 percent of the enrollees.

Phencyclidine

Phencyclidine is a white crystalline solid. On the streets, phencyclidine is called PCP, THC, or "Angel Dust." Burns and Lerner (1976) provide an excellent overview of phencyclidine's pharmacological properties and clinical implications. They note that it acts on the nervous system by either stimulation or depression and that this variability in action makes it difficult to classify.

Phencyclidine can be swallowed (generally in tablet form), snorted (insufflated), or smoked (inhaled). Among the young people we worked with, snorting and smoking are the preferred routes of administration. When the drug is smoked, the user spreads the phencyclidine over marihuana, parsley, mint, or tea. This is called a "crystal joint." The time course and active effects of phencyclidine vary as a function of the concentration and the route of administration. The users we have spoken with stated that the "hit" time ranges from five to twenty minutes. Snorting results in a faster action, and, in the opinion of some individuals, it produces more side effects than smoking.

Phencyclidine is purchased by the "line." A "line" is about 3/4 of an inch long and 1/8 of an inch wide. This amount sells for around $10 to $15 in Honolulu and is enough for five users or "hits." The concentration of the phencyclidine is determined by the number of visible crystals present among the filler. The users indicated that phencyclidine is only available from dealers periodically, but when available it is very popular.

Who Uses Phencyclidine?

Because our experience with phencyclidine users is limited to Job Corps enrollees, we clearly have no information regarding the community distribution of phencyclidine use in Hawaii. However, based on the comments of the Job Corps users, we are inclined to conclude that the highest frequency of use is among preteen and teen Hawaiian youth ("locals"). Everyone we spoke with indicated that Micronesians and Guamanians prefer "hard liquor" and "grass" rather than "T." They indicated that there is some use of "T" among Samoans and Filipinos but that the highest use was clearly among the "locals." Indeed, they noted that "T" was growing in popularity among "local" kids and that they could not think of any "local" friends who had not tried it. Although the Caucasian youths use it, "T" does not seem to have much popularity among them.

The high frequency of phencyclidine use among "locals" as opposed to other groups raises some important questions about the reason for this state of affairs. Our speculation is that among "locals" the use of all drugs is much higher and more flagrant. Thus, a new drug like phencyclidine simply fits in with an already existing culture of users, and other ethno-cultural groups are often excluded from these "local" drug-using groups. Indeed, some of the other ethno-cultural groups look on the "locals" as being crazy when it comes to taking drugs; the other groups describe themselves as liking to drink a lot of booze and smoking a lot of grass, but they do not see this as being really harmful, even though they often consume entire bottles of liquor among a few users.

In addition, it is our observation that the "locals" seen to have the greatest ethno-cultural identity problems. The other groups still use their native languages and follow many of their traditional customs. This is not true of the "locals" who are English speaking and who are often unsure of their allegiance to Hawaiian culture, although they describe themselves as Hawaiian. Their identity is much too superficial to provide a perceptual framework for mediating life problems. The "local" youth are clearly the most alienated and lacking in a sense of purpose and direction when compared to other youth in the Job Corps.

Lastly, anger levels are extremely high among "locals" because of their discontent with their social position. Unlike the Micronesians, Guamanians, and Samoans, the anger among the "locals" is long term. "The Hawaiian people are getting shafted in their own land" is a widely shared belief which seems to be constantly reinforced by family and media. Further, ability of the "locals" to articulate their problems and to attribute them to their status as Hawaiians provides a strong self-reinforcement of their anger. The possible role of anger in phencyclidine abuse will be further discussed in the next section of this paper.

WHY IS PHENCYCLIDINE ABUSED?

It is tempting to say that any drug with consciousness-altering properties is likely to be abused by today's youth if it is available. However, this type of thinking is much too general to account accurately for the preferences and patterns of drug abuse which have developed. It may indeed be the case that each drug has a unique pattern of situational and personality factors which both encourage and maintain its abuse profile. In discussing the reasons for phencyclidine abuse, we will comment on three topics: (1) Situational, (2) Experiential, and (3) Psychosocial.

Situational Factors in Phencyclidine Abuse

Everyone with whom we have spoken told of being "turned on" to phencyclidine by close friends who simply said, "Try it...it will make you feel good!" Quite obviously, the social pressure to go along with this soft sell amidst a group of friends is quite high. To refuse is tantamount to saying you don't trust your friends or that you are afraid. Both of these are higher risks than the dangers associated with a new drug. Among young people with fragile or vulnerable self concepts, the pressure for acceptance simply outweighs the pressures of rational judgment regarding the harmful sequelae. The group dynamics are critical in getting started and in maintaining drug abuse with a substance like phencyclidine.

Phencyclidine use is not limited to a particular environment. It is used indoors with mellow music and candlelight, and in noisy settings with rock music and flashing lights. It is also used outdoors at parks and beaches. Indeed, several people discussed going swinming while on "T" and almost drowning. However, everyone indicated that the mood of the user is important in determining the reaction to the drug. You can get "spacey" or "mellow" or you can just get "stoned." But, quite interestingly, everyone said they always used "T" in a group rather than alone. This may not be unusual, as many drugs are taken in group settings, but it does deserve further study.

Experiential Aspects of Phencyclidine Abuse

A young "local" female with years of polydrug experience described phencyclidine as "the — [worst] snortin' drug you can ever take!" Yet, when asked if she would take it again she replied, "Sure...why not?" We have been continually impressed with the almost total disregard for any of the medical or legal consequences of drug abuse among many of the "Local" youth in Hawaii. They simply say, "Man, who cares!" or just smile and shrug their shoulders and say, Wan, ain't no big thing!" Booze, grass, and "T" are mixed readily. We never heard anyone, however, speak of mixing acid (LSD) or speed and "T". It is also interesting that the users seem to categorize "T" as a hard drug: many said it gives a "rough trip."

Efforts to understand the actual phenomenological experience associated with phencyclidine have always proved frustrating be-Cause the users tend to describe the experience in short phrases like 'Wowie!," "Cloud nine!," "Far out!," or "Zap!" These phrases are often accompanied by a throwing back of the head, a rolling of the mouth in an almost reflexive manner.

Several individuals told us to "try it" to really understand what it does because "you can't put it in words." "Being stoned is something else!" We have speculated about whether the actual subjectivity and privacy of the experience might in itself be rewarding. "You can't put it in words!" Here is something which is truly yours, something which is unique and not subject to loss through intellectual understanding. In a world of intruding influence, here is something that belongs to you. A few males and females likened the "T" experience to that of "surfing all day" when because of the repetitive excesses of sensory stimulation and deprivation you come to lose your sense of self and become a part of something more - the endless rhythm of waves.

On the other hand, if you take too much "T" you are really in for it. It is much more than just "flipping out." One male described his experience under a high dose as being similar to "electric man." His entire body was numb and paralyzed and he tingled all over. He recalled praying to God and saying "Please don't let me die." Yet in spite of the experience he took "T" again. It was his fault, not the drug's. Another male said he felt like a "zombie"; but he also used it again.

When used in smaller doses or concentrations, the youth described the sensation of their body becoming "very light" or "floating," almost as if they were "walking on air." This is the pleasurable sensation that they like and seek. One individual suggested it was very similar to inhaling "laughing gas" in the dentist's office. Another individual indicated that it made him see things. He noted that on one occasion he thought he was body surfing and extended himself on the rug as if he were riding the waves. Yet another person said he liked seeing the "dragons" and "creatures" when he was on "T."

Apparently, the "T" experience is also a function of how often you take the drug. A male "local" who was experiencing visions and was becoming quite afraid reported "talking with angels" and "see- dead relatives." He also stated that he believed that he was really "someone special" with unique "powers." At first, he denied taking any drugs stronger than grass, and so we were inclined to suspect that an incipient psychotic process was operating. However, when he was asked if he had been taking "Angel Dust," he said that he was using it in "joints." He was asked to stop this immediately and to refrain from using it any more. He agreed to stop, and within. two weeks the hallucinations had disappeared and he was no longer afraid.

Although some of the young people we have worked with have beams belligerent and antagonistic under phencyclidine, we know of one case where violence occurred. This case was reported by a user and involved a young "local" female who had been using "THC" for "breakfast, lunch, and dinner" over a period of a week. The girl dug out the cheeks of her little infant's face and then told her mother, "Look what the devil did to my baby." A number of users have talked of "T" users becoming "religious" after a while. However, they were unable to explain why this happens. They simplY said if you use "T" for a while you become a "Jesus freak" and "get turned on to religion."

Most of the people we have spoken with stated that they preferred to take "T" in quiet places where they could just "space out." One individual said, "No feel like walkin', no like talkin', just sit back and look." When talking does occur under phencyclidine, it was described as being slow and drawn out. On higher "hits" they reported having difficulty walking. One person reported falling down and described it as a "slow motion" experience in which each movement took a very long time.

None of the people with whan we have worked could be considered a phencyclidine "freak," that is a person who chooses only phencyclidine when given a choice. Indeed, everyone agreed that they had never encountered a "T freak" as they had encountered "acid heads" or "speed freaks." People appear to use "T" when it is available. It is just one of many drugs that can be used if you want to "trip." Several people, however, said that "T" is better than "booze" or "downers" if you want to trip out because it is faster and stronger. They stated, "When you wanna git away, "T" is good"; they noted that it "takes your mind off things and lets you relax." In those circumstances, "T" is the preferred choice; they start with grass and then snort a "hit" of "T."

In addition to the medical risks of a high dose, "T" users must also cope with the side effects which accompany its use, even if the dose is mall. Some people described the effects as being similar to a hangover. They feel "wobbly" and "queasy" and have headaches around the front of the head. Vomiting and dizziness are also quite common. They all agreed that they were very tired and wanted to sleep. One person said he felt "wasted" and "run down." But, these are not very different from side effects associated with drinking too much, so they are considered worth the risk.

Psychosocial Aspects of Phencyclidine Abuse

The medical aspects of phencyclidine intoxication will not be discussed here, since these have been very well presented in a number of papers by Burns and Lerner (1976), Burns et al. (1975), Eastman and Cohen (1975) and Linden, Lovejoy, arid Costello (1973). How ever, there are several psychosocial aspects of phencyclidine abuse which deserve comment. These include the role of chronic feelings of anger and desperation, the role of agitated boredom, and the results of conditioning deviant epistemic orientations.

1. **Chronic Anger and Desperation**

Over the years, we have increasingly wondered about the effects of the chronically high levels of anger and desperation found among many of the Hawaiian youth with whom we have worked. We are reminded of the effects which "low status" and "enduring frustration" have had on black Americans, the so-called "black rage." The "local." people appear to be relatively helpless in altering their own lives in the face of the continued onslaught of Western technology and values presently occurring in Hawaii. Their way of life is demeaned. In the search for an escape from their feelings of desperation, they see themselves as having few alternatives. Freud, in his book _Civilization and Its Discontents_, wrote:

> Life as we find it is too hard for us; it entails too much pain, too many disappointments, impossible tasks. We cannot do without palliative remedies....There are perhaps three of these mans: powerful diversions of interest...substitute gratifications...and intoxicating substances.

In the absence of diversions of interest and substitute gratifications, intoxicating substances have emerged as the most available and effective mans for handling the annipresent tensions of anger and desperation. Both of these require expression, release, or catharsis. Assault and other forms of violence have already resulted in high rates of delinquency and crime among the "locals," and excessive drinking is also a major problem. To both of these inadequate ways of coping must now be added the drug phencyclidine. Here is an easy and quick way to relax, to remove the omnipresent burdens of anger and desperation. Relief is just a snort away! It's a magical release from life's pressures even though it only lasts a short while. These points lead us to the role of boredom.

2. Chronic Boredom

In a society which requires ever increasing levels of competence and specialization to achieve recognition, success, and financial reward, more and more individuals are finding that there is little they can do. Many young people are simply retreating and withdrawing from societal demands rather than facing the challenge of coping with life through the active pursuit of a skill or education. Indeed, it is quite obvious that our society simply asks youth to wait their turn to make any meaningful input. Youth are not given a chance to be adults. They must wait and learn. But, when the learning experience offered by our schools is sometimes so vacuous, there is only boredom.

Boredom is a problem which more and more young people are experiencing, and it is also one which is readily dissipated by a "hit of T." There is little opportunity for our youth to feel important and meaningful, and this problem is compounded for "local" youth because of theirlowstatus and imprboble chances for altering their poverty. Boredom, like any other aversive affective state, requires relief: and in the absence of alternatives, "T" serves the purpose quite well.

Yet, we are coming more and more to wonder whether the quick escape promised by "T" is not exacting its toll. Here, we would speculate that the deadening of experience or the alteration of conciousness somehow produces a subsequent need for arousal. It is tempting to believe that the nervous system requires periods of arousal and periods of rest. An extended period of one leads to a need for its opposite. Thus, we would speculate that, with continued phencyclidine use, a cycle may be developed of increased agitation and arousal when the drug is not in use. This could be experienced as an undifferentiated emotional state of boredom. And so the cycle of "stimulus reduction" and "stimulus seeking" continues. Every "hit" of phencyclidine my require a subsequent period of arousal or of undifferentiated alertness.

In the absence of a meaningful pursuit of some knowledge or skill, agitated boredom emerges. If an incident should occur which might be interpreted as hostile, the agitation simply comes to be interpreted as anger, and an acting out occurs even if it is unwarranted.

This cycle has yet another aspect which may ultimately prove to be more dangerous. This latter aspect involves the conditioning of deviant epistemic orientations.

3. The Conditioning of Deviant Epistemic Orientations

There are some individuals who argue that the judicious use of drugs should not cause alarm (e.g., Szasz 1972; Reinert 1974). They claim that ethically we may not have a right to deprive people of pleasure-giving drugs. Reinert (1974) stated:

> What is our right to take away pleasure-giving drugs from a person who through early deprivation, or current poverty, or lack of training, or lack of innate capacity has little capability for pleasure in aesthetics, intellectural pursuits, or social intercourse?... Are we morally justified in depriving an individual whose life is without purpose, hope, and direction--cramped, lonely, and bitter--of the chief pleasure of which he is capable? (Reinert 1974, p. 56).

In the case of phencyclidine use among "local" youth in Hawaii, Reinert's comments raise some interesting questions, especially within the context of the social deprivation to which they are ordinarily exposed. Yet, there is a risk which Reinert is ignoring, and this is the conditioning of deviant epistemic orientations which may ultimately make it impossible for an individual ever to accomodate his life and thoughts to societal expectations and demands.

In a previous paper (Marsella and Price-Williams, 1974), it was argued that the continued use of consciousness-altering drugs posed an ignored danger: the conditioning of deviant epistemic orientations. An epistemic orientation involves certain conceptions of time, space, and cause-effect relationships. Through the course of normal everyday life within a particular cultural context, an epistemic orientation is created which is functionally related to other cultural forms and practices. For example, in our own society we have a shared notion of time, space, and cause-effect that n-takes it possible for us to function "normally."

The nervous system codes time, space, and cause-effect experiences regardless of the consciousness level at which they are experienced. This means that even on a drug which alters consciousness, the nervous system is still coding these epistemic dimensions:

> The experiences of the "trip" are no less real to the nervous system than those of everyday "normal" life. The "trip" experiences are assimilated, coded, and organized into existing cognitive and neurological structures. Thus, over long periods....of use, the person develops a new and conflicting epistemic organization that extends beyond the actual drug states.... (Marsella and Price-Williams 1974, p. 71).

In brief, with continued use of phencyclidine, the users may soon find himself/herself experiencing reality according to levels of consciousness which are in conflict with normative standards. His/her sense of time, space, and cause-effect become deviant. New standards of "normality" emerge which are not shared, thus fostering deviancy and furthering the rejection cycle.

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Chapter 11

The Pharmacokinetics of Phencyclidine in Overdosage and Its Treatment

Alan K. Done, M.D., Regine Aronow, M.D., and Joseph N. Miceli, Ph.D.

The unusually prolonged and vacillating clinical course of PCP intoxication has been documented amply in other parts of this publication and in citations included elsewhere (Done et al. 1977; Aronow and Done 1978). Except for the demonstration of persistence of urinary PCP excretion for at least several days in some cases (refs. cited in Done et al. 1977) there had been no explanation for that finding or the clinical course, and certainly no definition of the pharmacokinetic characteristics of PCP in overdosage, until our recent studies (Done et al. 1977). This report supplements the earlier preliminary observations with extensive additional observations which are soon to be published inconsiderably more detail.

SUBJECTS AND METHODS

Data presented here were obtained from seven patients whom we treated for PCP overdosage; further clinical information about them is presented by Aronow elsewhere in this publication. All patients took unknown quantities of "street" PCP in various form, and its identity and purity were established on the material itself and/or the gastric contents by gas chromatography/mass spectrometry as described elsewhere (Done et al. 1977). The procedures for obtaining the blood, urine and gasttic fluid specimens were also described previously. The present protocols varied somewhat from the earlier ones and from patient to patient, particularly in terms of the duration of urine or gastric fluid collections, depending the aim of the particular study; however,continuous urine and gastric contents ware collected quantitatively; and blood specimens, insofar as possible, were obtained midway in these collection periods. An exception is patient 1, who did not have gastric suction because he presented before our studies had indicated the importance of this procedure.

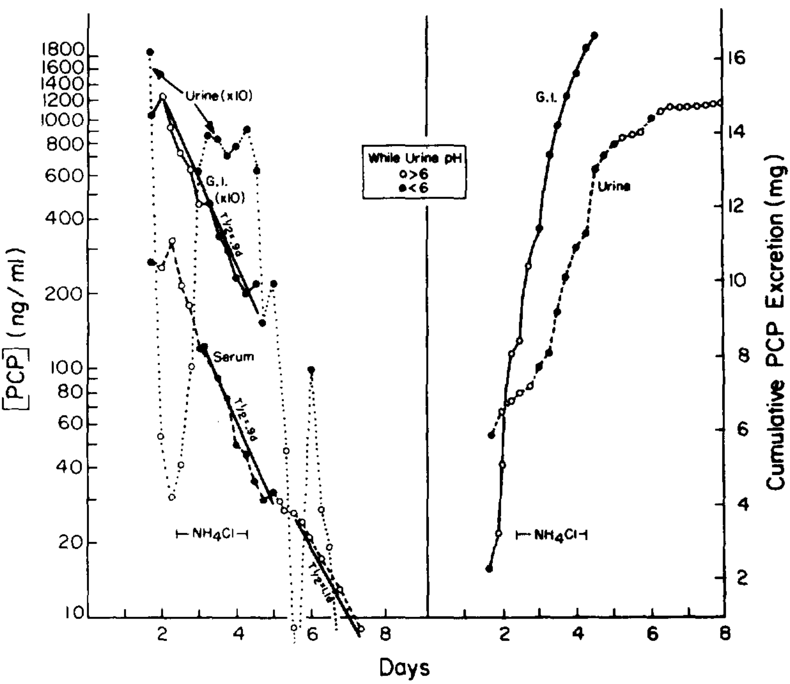
After our initial observations indicated the important influence of urine pH on PCP excretion, some patients were given acidifying agents in a manner described by Dr. Aronow (Aronow and Done 1978) and in some individuals furosemide diuresis was instituted,usually at time of peak acidification of the urine. All pH measurements on urine and gastric fluid were made immediately using a pH meter (Beckman model 3550), and in arterial blood with a conventional clinical blood gas electrometer.

Specimens were frozen until analyzed for PCP concentrations by Dr. Denis Lin of Battelle Columbus Laboratories using his gas chromatographic/chemical ionization mass spectrometric method (Lin et al. 1975). Measurements were confined to the free,unchanged compound.

RESULTS

Figure 1 shows (on the left) the time course of serum PCP concentrations and its relationship to PCP levels in urine and gastric (G.I.) fluid. It can be seen that the gastric fluid [PCP]

FIGURE 1



[PCP] in serum, urine and gastric drainage (left) and cumulative urinary and gastric secretions of PCP (right) in a representative patient. In the left half of the figure note that a log scale was used, and urine and gastric (G.I.) concentrations were 10x higher than shown (Done et al. 1977).

is very much higher than that in serum, and that the two curves are strikingly parallel and have similar half life (T½) values. The T½ varies considerably from patient to patient and, as will be noted below, is strongly dependent upon whether or not there is interruption of the gastroenteric recirculation of PCP; consequently, half life figures will be reserved until discussion of this phenomenon. As will be discussed in considerable detail later, the urine PCP concentration was strikingly dependent upon the urine pH and so bore a variable relationship to the serum level; however it also can be considerably in excess of the concentration in serum. That is to say that PCP is highly concentrated in an acid medium, which can cause it to achieve a tremendous gradient with plasma. The cumulative excretion data (the right half of the figure) indicate that in some individuals the elimination by way of gastric suction can, for a time at least, substantially exceed that achievable through urinary excretion, though this is highly variable from one patient to another.

That the pH effect on PCP concentration gradients is reflected in in a similar effect on clearance is indicated by table 1. The clearance figures are not identical with those presented by Dr.

TABLE 1

EFFECTS OF pH ON (PCP) PLASMA GRADIENI

AND PCP CLEARANCE, $\frac{\text{Mean} \pm \text{SEM}}{(n)}$

	Gastric		Urine		
pH:	<2.5	>2.5	<5	5-6.5	>6.5
(PCP)/(PCP)p	42±4.5 (42)	20±3.8 (20)	97±17.4 (19)	36±5.0 (60)	7±2.4 (32)
Clearance ml/min)	53±11.2 (44)	21±5.0 (15)	86±15.0 (19)	44±6.6 (59)	10±2.4 (31)

Aronow because the data presented here include only those individuals who had exactly simultaneous collections of blood and the other fluids under study; some of the clearance values presented by her utilized interpolated serum level estimates when the curves were sufficiently smooth that there was no sacrifice of accuracy. Here it was desirable to compare simultaneous effects on the gradient with serum concentration and the clearance. An interesting phenomenon with regard to gastric secretion of PCP is that pH influence appears to be somewhat less striking than it is with urine on the basis of extrapolation of the urine pH data. There is ample precedent for such an observation provided by Brodie and Hogben (1957), who found that most of the basic drugs studied were incapable of being concentrated in the acid medium of the stomach beyond maximum of about 40 times that in serum(about the gradient that we see here), a phenomenon that in the dog was found to be attributable to limitations on circulation of the drug to the gastric mucosa. In other words, the nonionized fraction of the drug was cleared with a single passage of blood through the stomach's circulation and so the gradient of clearance was limited by the bleed supply.

The present and our earlier observations (Done et al. 1977; Lin et al. 1977) suggest that the effect of pH cm PCP distribution is a truly tremendous me, probably due to an effect on ionization of this weak base thought to have pK_a, of about 8.5. The remainder of this discussion will be devoted principally to further exploration of this conceptandits possible therapeutic implications.

The relationship of pH to urinary excretion of PCP is variable from one patient to another and possibly influenced by a number of factors, butatleastin some the evidence supports a pure ionization effect (Done et al. 1977). To the extent that we are dealing with an ionization effect and ion trapping in more acid, media one would expect pH influences on more than just the products of excretion. Further,such effects should be interrelated and produce a somewhat predictable net result which might have important clinical implications. While limited access to the various other tissues, fluids, and compartments in the human is an obvious obstacle to full explorations along these lines, considerable can at least be surmised about some of the redistribution consequences. Table 2 shows some representative data obtained from a patient at two points in time

TABLE 2

pH EFFECTS CN PCP DISTRIBUTION *

	pH	(PC) ,ng/ml		pH
Serum	7.4	66	50	7.2
CSF		140	8	
Urine	7.5	43	3997	5.0
Stomach	1.4	1395	1287	2.2

*patient 5, ammonium chloride acidification

when spinal taps were performed because the clinical picture could not exclude other intracranial pathology. One would expect acidification of plasma to result in considerable outflow of PCP from the central nervous system, comparative trapping in the plasma, and, to the extent that the urine becomes acidified in the process, also a striking increase in excretion. Such can be seen here where a drop of serum pH from 7.4 to 7.2, caused by ammonium chloride administration, resulted in a decline in the cerebrospinal fluid PCP concentration from more than twice to less than 1/6 that in serum. During this time the serum level declined only slightly, considerably less than would have been expected from the tenfold increase in urine PCP concentration (and clearance),possibly because of shifts of nonionized drug to plasma from less acidic compartments (such as the central nervous system). In any event, these figures indicate the ability to achieve desired shifts in PCP distribution and enhancement of excretion through pH manipulations. Incidentally, these shifts even within the body are associated with striking and immediate improvement in the CNS effects. Also, if you remember that the markedly enhanced urinary elimination of PCP can be accompanied also by elimination of that amount in the stomach through the simple expedient of gastric suctioning, it can readily be seen that the net result is expected to include the substantial shortening and improvement of the overall course that we and others have noted. Further,as is discussed by Aronow, induced diuresis superimposed upon urine acidification substantially augments still further the urinary excretion of PCP.

From the gastrointestinal standpoint, with the involvement of pH in determining ionization of a weak base such as this, and its ion trapping in the stomach, the expectation must be that there is substantial gastroenteric recirculation of the drug. After it leaves the acid of the stomach it would be expected to become relatively less ionized in the more alkaline intestine and there fore to be reabsorbed, and this would be fully expected to play a role in determining the course, particularly the duration, of PCP intoxication. When the time course of serum PCP is followed it is found that discontinuance of previously constant gastric suctioning is associated frequently with an immediate rise in serum [PCP], its strikingsubseqent fluctuation, and a substantial slowing in the rate of disappearance from the circulation. Table 3 compares serum [PCP] data obtained during and after discontinuance of constant gastric suctioning: the change of serum concentration immediately

TABLE 3

GASTRIC SUCTION AND COURSE OF SERUM [PCP]

Pt.	Immediate k_e (da^{-1})		"Post-absorptive" $T_{1/2}$ (da)	
1	-	-.2	-	3.0
2	-.4	-.02	1.6	3.2 +
3	-.9	-.3	0.9	1.2 +
4	-.5	+.9	1.1	-
5	-.8	+.9	1.2	3.0 +
6	-.99	-.3	0.9	1.8 +
7	-.6	+.8	1.1	1.0
Mean	-.7	+.25	1.1	2.2 +

Gastric suction stopped

before and after discontinuance of gastric suction is shown as a daily rate or k_e on the left; the "post absorptive" serum concentration half life measurements -- i.e., after serum concentrations, either initially or upon discontinuance of gastric suctioning, have begun to fall -- are shown on the right. Half life values followed by a + are minimal ones because striking rises in serum concentration (common after discontinuance of gastric suction) were not included in the detemination; had they been, the apparent effect of gastrcenteric recirculation of PCP on serum half life of the drug would have been even greater than shown. It can be seen that in all patients the elimination rate immediately after cessation of gastric suctioning, compared with the one immediately before,was slower or was apparently overridden by increased absorption from the gastrointestinal tract so that the level actually climbed.

In all but one case where the comparison could be made, the serum concentrationhalf life of PCP was considerably longer without gastric suctioning than with it. On the average, there was more than a doubling, even if we ignore the striking rises that often occurred long after discontinuance of suctioning. It should be noted that the serum concentration T½ in untreated patients must be assumed to be longer even than those shown here on the right (table 3) not only for the reasons mentioned, but also because all patients except 1 and 2 in this series were subjected to therapeutic urine acidification. The natural serum concentration T½ would appear to be over 3 days at the concentrations encountered here.

DISCUSSION

The finding of an appreciable gastroenteric recirculation of PCP helps to explain the prolonged course of intoxication from this drug. This and the strikingeffects of pH on distribution in various compartments, may well explain the notable vacillations in the clinical course mentioned previously. These observations also suggest a course of therapy that has been applied with the dramatic success described by Aronow in this publication, and in earlier reports by this group (Done et al. 1977; Aronow and Done 1978).

The urinary excretion of trapped PCP is so striking that, as is discussed by Aronow, the efficiency of peritoneal dialysis with or without added albumin is dwarfed by the results that can be obtained with highly acidified urines. Whether extracorporeal hemodialysis would be more efficient and whether it could be augmented by any safe and reasonable manipulations of the acidity of the dialysis fluid remains to determined; this could be a very important consideration in patients with renal insufficiency. We have had no personal experience as yet with this particular problem, but this possibility certainly deserves exploring and in the meantine the role of peritoneal dialysis and certainly that of gastric suctioning would take on added potential importance in patients having poor kidney function.

The gastric trapping of PCP has important forensic implications. The drug is often smoked and occasionally is injected, but it would be expected to appear in the stomach in large quantities regardless of the routeofadministrationand such a finding should not be interpreted as evidence of oral ingestion.

We are not aware of other basic weak electrolytes whose distributions are so profoundly affected by pH manipulations. However, few bases (as contrasted with acids) have been so evaluated. Hence, it is quite possible that ion trapping is mode of therapy for poisoning with such compounds that has received inadquate attention and deserves further exploration (Done 1976). We currently are actively exploring this possibility while also exploring additional parameters of PCP pharmacokinetics that may provide a basis for still more improvement in treatment.

The analytical method used in this study measures only unchanged PCP, so the results are informative only with regard to the parent drug. However, the hydroxylated derivatives known to be pruduced by humans have not been demonstrated in the blood, apparently because they are converted to the glucuronides and excreted as rapidly as they are formed. All of the urinary metabolites are present as the glucuronides, and there is extensive excretion of the free, unchanged drug. Thus, studies of the partent compound alone probably suffice to define the toxicologically important kinetic parameters; however, studies of the metabolites as well are required before this concept can be accepted without reservations. Such studies are currently underway in this laboratory.

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Chapter 12

Clinical Observations During Phencyclidine Intoxication and Treatment Based on Ion-Trapping

Regine Aronow, M.D., Joseph N. Miceli, Ph.D., and Alan K. Done, M.D.

Since technology to detect phencyclidine (PCP) in body fluids became available to us, fifty cases of PCP overdose have been treated at the Children's Hospital of Michigan. The patients ranged in age from nine months to almost twenty years. Preliminary observations in overdosed adolescent boys of the pharmacokinetics of the drug (Done et al. 1977) have led us to successfully treat a number of severely overdosed patients utilizing ion trapping by continuous gastric suctioning and acidification of urine and/or blood with ammonium chloride (Aronow and Done 1978). Although many of the children under eight years of age presented after rapid onset of coma, only three seemed of sufficient severity to require urine acidification in addition to continuous gastric suctioning and supportive care. We have, however, no quantitative data on young children. This report offers additional data on seven patients above the age of thirteen years who are being studied in detail and who are also discussed in Dr. Done's paper in this volume.

BACKGROUND

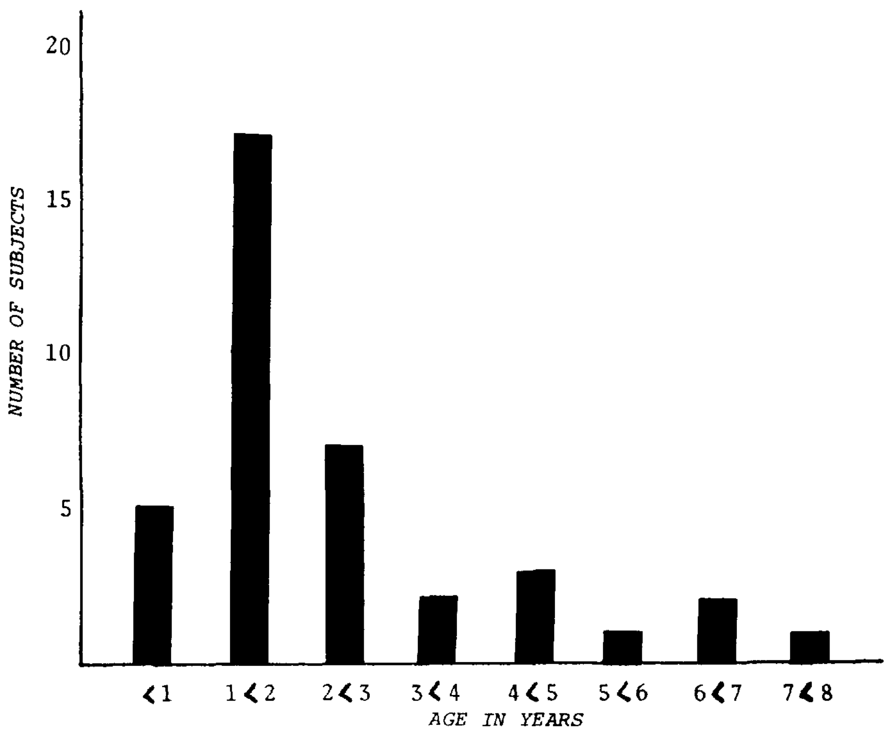
In the early 1970's a number of small children with symptoms now recognized as associated with phencyclidine overdose were seen at the Children's Hospital of Michigan, supposedly having ingested street drugs, variously representedas THC, mescaline or LSD. Paper chromatography spot tests done elsewhere failed to reveal the presence of narcotics, sedatives or tranquilizers commonly used in our area. Beginning in December 1972, arrangements were made with a private research laboratory to screen blood and urine samples on selected patients for mescaline, LSD and PCP, the latter having been brought to our attention by the Drug Enforcement Agency. By mid 1974 an emergency service utilizing a GC-MS system became available (Horowitz et al. 1976) and urine, gastric and blood samples have since been submitted there for initial screening. Retrospectively, we learned that although this system would identify large amounts of PCP, the injection temperature used could destroy small amounts of PCP (personal communication, Dr. Lin, 1978). Thus we may have missed some cases.

All cases of PCP overdose referred to in this paper gave positive evidence of PCP in body fluids by one of the methods mentioned above.

EPIDEMIOLOGY

Our experience with children younger than eight years of age (figure 1) shows an age distribution not unlike that of accidental poisoning in general (National Clearinghouse Bulletin 1977), an indication of the fact that the drug was commonly in their environments and subject to being ingested by the children. Social service investigations revealed someone may have purposefully administered the drug to two of the children. All the cases had child abuse/neglect filed.

FIGURE 1



There were no cases recognized in the eight to thirteen year age range.

Total patient data reveal an equal distribution between males, females, blacks and Caucasians in the under eight years of age group, but a disproportionate number of Caucasian males in the 13 to 20 year old group (tables 1, 2).

TABLE 1

Patient Experience: Dec. 1972 - Feb. 1978

AGE (yrs.)	SEX		RACE	
	M	F	B	C
<8	20	18	18	20
13-20	10	2	1	11

TABLE 2

Patient Experience: Dec. 1972 - Feb. 1978

AGE (yrs.)	SEX by RACE			
	BF	BM	CF	CM
<8	8	10	10	10
13-20	0	1	2	9

In the early calendar years included, there was a fifty percent greater incidence of black children identified with PCP overdose than of Caucasian children. This has reversed in the last year to sixty-six percent Caucasians (table 3).

TABLE 3

Patient experience (AGE vs RACE)

CALENDAR YEARS	AGE (yrs.)	No.	BLACK	CAUCASIAN
1972(1 mo.) 1973 1974	<8	10	8	2
	13-20	2	0	2
1975	<8	12	5	7
	13-20	2	0	2
1976	<8	5	2	3
	13-20	3	0	3
1977 1978 (1 mo.)	<8	11	3	8
	13-20	5	1	4

Only rarely are adult PCP overdose cases seen at Detroit General Hospital, the major inner city emergency service, which gives credence to the race distribution. Most of the older Caucasian patients seen at our hospital have come from communities other than Detroit.

SUBJECTS AND METHODS

The clinical courses of eight patients are given in summary form in table 4. Patients 1, 2 and 3 were described previously with their pharmacokinetic data (Done et al. 1977). The varying symptomatology associated with PCP overdose has been described by many authors and is tabulated and referenced in our previous publication (Aronow and Done 1978).

Patient 4 was treated at another hospital with a representative of our group in attendance from six hours to 36 hours after admission. Quantitation of phencyclidine in his blood was done at a different laboratory (Domino and Wilson 1977) than his gastric secretion and urine. These were analyzed along with all specimens from the other patients, as previously described (Done et al. 1977).

Patient 8 presented in an acute psychotic state after taking repeated doses of PCP over a Period of one to two weeks. Only limited specimens were obtained and the patient's clinical course was actually biphasic. He showed dramatic improvement after twelve hours of ion-trapping, with his personality becoming intact. All therapy was discontinued, only to have his psychosis resurface in 4 hours. Therapy was again instituted, resulting in fluctuating improvement until 53 hours into therapy, when he regained normalcy. Modified therapy was continued until discharge five days later. On the third day post discharge the patient became agitated and paranoid, so he was rehospitalized and transferred to a psychiatric service. Unfortunately no studies were done on his second admission.

Methods of collecting specimens and their treatment are described in Dr. Done's paper in this volume.

The lowest serum PCP levels collected within 2-3 hours of consistent improvement of the patients' sensorium are given in table 5. Although the levels were taken at very diverse times in relation to estimated time of PCP ingestion, there is a rather striking similarity in the levels. It is not surprising that patient 5, with the longest period of coma, had a lower serum level. This will be discussed in detail later.

TREATMENT

Principles for treatment of PCP overdose at varying levels have recently been described (Aronow and Done 1978). In addition, careful examination for coexisting injuries should be made, as these patients are at high risk.

Patient 1 came to us late in his course and was given protective and supportive care until obvious symptomatology disappeared. Patient 2 was in consistent coma with repeated convulsions and severe laryngospasm requiring tracheal intubation for five days. He was maintained

TABLE 4

PHENCYCLIDINE OVERDOSE
Patient Data

Patient	Age (Yrs/Mos)	Weight (Kg)	Serum PCP, ng/ml (interval post-ingestion) at admission[a]	peak measured	Clinical Manifestations	Duration (from time of ingestion)	Treatment[b] (time from admission
1	13/11	40	74	Same	coma, $\uparrow$ tonus	4 hr	None
			(2.5 da)		halluc., nystag.	8 hr	
					disorient., $\uparrow$ acusis	3- 4 da	
					EEG abnormal:		
					delta rhythm	7- 9 da	
					dysrhythmia	9+da	
2	14/0	53	100	210	convulsion, $\uparrow$ tonus	3 da	Gastric drainage
			(0.5 da)	(1.0 &	coma	4 da	Peritoneal dialysis
				2.2 da)	laryngospasm	2- 7 da	Tracheal intubation
					halluc., agitat.	10 da	Diazepam (frequent)
					disorientation	15 da	Methicillin
					EEG abnormal:		
					delta rhythm	8-10 da	
					dysrhythmia	10-14 da	
3	18/0	45	264	329	coma, $\uparrow$ tonus	2.5 da	Gastric drainage
			(1.8 da)	(2.3 da)	agitation	3 da	NH_4CL
					disorientation	5 da	Ascorbic acid
					EEG abnormal:		Diazepam x 1 d 2
					delta rhythm	3- 8 da	Furosemide, 40 mg
					dysrhythmia	8+da	IV, d 1.3
4[c]	23/0	70+	92	182	coma, shallow resp.	12 hr	Intubation, .9 d
			(0.8 da)	(1.0 da)	nystag., agitat.	30 hr	Gastric drainage
							NH^4CL
							Ascorbic acid
							Diazepam x 1 d 1.3
							Furosemide, 40 mg
							x 2 d .9 & 1.3

TABLE 4 (continued)

STAGES	I PCP ACUTE TOXICITY	II PCP TOXIC PSYCHOSIS	III PCP PRECIPITATED PSYCHOTIC EPISODE	IV PCP INDUCED DEPRESSION
SIGNS AND SYMPTOMS	4 C's combativeness catatonia convulsions coma Hypertensive crisis Illusions and hallucinations Assaultive and/or self-destructive behavior	Impaired judgment Delusions Paranoia Hallucinations Flattened affect	Paranoid Schizophrenic like thought disorders with paranoid features	Depression Cerebral dysfunction
RECOMMENDED TREATMENT	Supportive medical management *$\downarrow$absorption $\uparrow$excretion Rx seizures and hypertensive crisis *antipsychotic medication *sedative medication	Residential Care *antipsychotic medication *sedatives	Residential Care antipsychotic medication	Outpatient therapy *tricyclic antidepressants medication
TIME	0-72 hours +	24 hours-7 days+	1 day-30 days+	1 day-several months
LABORATORY	Blood + PCP Urine + PCP	Blood - Urine +	Blood - Urine -	Blood - Urine -

* Use of these agents and procedures is open to question.

TABLE 5

PHENCYCLIDINE OVERDOSE

Lowest Serum Levels (ng/ml)
Related to State of Sensorium

Patient	Transferred CHM Approx. Time After Ingestion	Coma	Semicomotose	Disoriented
1	2.5 days	?	?	<42
2	7 hours	125	95	25
3	24 hours	125	95	25
4	? (Another Hosp.)	114	68	?
5	9 days	71	63	23
6	31 hours	130	109	24
7	23 hours	132	61	22.4
8	Chronic Use	–	–	<1.83

on gastric drainage, initially to reduce aspiration hazard, and then on a theoretical basis in hope of removing PCP if the tube advanced to the duodenum. No consideration of the possibility of ion-trapping in an acid medium was given at that time. Faced with the severity of the patient's symptoms, and a dearth of pharmacokinetic data on PCP, peritoneal dialysis was undertaken in a heroic effort over 72 hours, without obvious clinical improvement. Slowly, by the fourth day, coma became semicoma, which changed to disorientation on the seventh day, lasting for another week. The patient fully recovered.

Analysis of the data obtained from this patient's blood and urine samples revealed that PCP clearance seemed to be pH dependent (Done et al. 1977; Lin et al. 1977).

Patients 3, 4, 5, 6 and 7 all presented with coma of varying durations. The approach to their therapy was based on ion-trapping with variations in the dosage and route of ammonium chloride used. To attempt to bring the urine pH to 5 or lower, the dose of ammonium chloride delivered down the gastric tube was 75 to 125 mg/kg (Edelmann et al. 1967; Chan et al. 1974) every six hours. This was diluted in 2 ounces of saline. If the patient vomited or had evidence of marked gastric irritation, the dose was sometimes delivered in two small increments one half hour apart. The gastric tube was then clamped for one to two hours before continuous drainage was reestablished. Most patients' urines converted to a pH of 5 or lower after the second dose.

Concurrently, ascorbic acid, varying in dose from 500 mg to 2 gms, was added to the intravenous fluids every six hours.

Particular attention must be paid to maintaining good urine flow (2 mg/kg/hr) by adequate intravenous fluids and electrolytes, especially potassium.

Once urine pH was at 5 or lower, furosemide (1/2 to 1 mg/kg) was administered. Often this was followed by a marked improvement in the patients' sensorium and symptoms. Repeat use of the diuretic was dependent on the patient's fluid balance as evidenced by the central venous pressure, and could probably be repeated more often than was done in these patients.

Patients 5 and 6 received ammonium chloride intravenously at a dosage of 2.75 mg/kg as a 1 percent or 2 percent concentration in saline (derived from Quadrate, a 21.4 percent solution of ammonium chloride) purposefully to lower blood pH so as to create a gradient with spinal fluid and hopefully clear the central nervous system and spinal fluid of PCP more rapidly. Blood pH fell in patient 5 before urine pH reached five, and the level of PCP in this patient's spinal fluid markedly decreased with concurrent clinical improvement.

Duration of gastric drainage was arbitrarily set at three to four days but in some patients was discontinued earlier because of nasal irritation and bleeding (patient 6), anxiety about gastric erosion from the ammonium chloride solution, and patient discomfort as clearing of the sensorium occurred.

In patient 7 betazole hydrochloride (Histalog) was used once to increase gastric secretions. There was no adverse effect reflected in blood pressure; however, there was no dramatic change in sensoriun following three hours of marked increase in volune and decrease in pH of gastric secretions.

Once the patients' sensorium had cleared and the nasogastric tube had been removed, ascorbic acid, two to eight grams in divided doses, was given daily as well as several glasses of cranberry juice (excreted as hippuric acid in the urine), to maintain an acid urine for at least another week.

DISCUSSION

Ion-trapping to enhance PCP excretion has been employed successfully in acute PCP overdosed patients, as evidenced by a lack of convulsions or hypertensive episodes once treatment is underway, relief of muscle hypertonicity, and steady improvement in sensoriun until out of coma (even after 9 days of coma). With careful attention to good supportive care, there have been no complications of therapy.

Cumulative data on these patients clearly show the influence of pH on clearance of PCP (table 6). Although peritoneal dialysis can clear some of the drug, it is the least efficient unless 5 percent albumin is used. With only two samples on which to make a judgment, we would reserve this treatment possibility for the patient with renal insufficiency.

Gastric suctioning may appear to be somewhat lower in efficiency than it is, due to several factors. Patient 5 generally had lower gastric clearance than other patients with her clinical severity, perhaps because of the long time she was in coma before ion-trapping was instituted, allowing for distribution of PCP into other body compartments. Also, from the pharmacokinetic data shown by Dr. Done elsewhere in this volume, it is evident that even clamping the gastric tube following ammnonium chloride instillation adversely affects the serum PCP level. We have also found that the pH of the ammonium chloride solution used is in the range of 4.5 and raises the gastric pH temporarily.

Histalog more than doubled the PCP clearance in the gastric secretion but requires further evaluation before being used routinely as a possible adjunctive approach, It may be especially helpful for patients with renal insufficiency. The observation that several of the young children who presented in coma regained consciousness immediately following gastric lavage is further evidence of the importance of the pool of PCP that may be in the gastric compartment.

Clearly the most dramatic increase in clearance occurs as urine pH dips to 5 or lower and furosemide is given. This probably accounts for the marked improvement that often occurs in the patients immediately following diuresis under these conditions.

TABLE 6

PCP CLEARANCE (ml/min)
(cumulative data on 7 patients)

	Mean	SEM	No. of Samples
Urine, pH> 6.5	7.0	± 0.70	34
pH 5 - 6.5	57.4	± 6.57	128
+ furosemide	(205.3)		3
pH < 5	134.5	±25.55	44
+ furosemide	(299.3)		7
Peritoneal dialysis	2.4	± 0.39	11
with 5% albumin	(4.1, 4.5)		2
Gastric suction	44.8	± 8.40	61
after Histalog	(95.7)		3
			278

Whether it is better to give furosemide when the urine pH is 5.5 or to wait to get it down below 5 is not quite clear. Perhaps utilization of another diuretic agent would be more efficacious. These are some of the refinements in the therapeutic approach that we have under study.

There are other methods to acidify urine, but we have preferred to use ammonium chloride. It is contraindicated, however, in anyone with liver disease. Three of the children under eight years of age have received one or two doses, as a gastric bolus, with successful acidification of urine to pH 5 or lower. Although we did not find evidence of hyperosmolarity in the patients given ammonium chloride intravenously, this treatment must be used cautiously in small children as they are exceedingly sensitive to hyperosmolar states.

Although all but one of the patients were considered acute overdoses, there was reason to believe at least three were regular members of the drug culture. No doubt chronic use of PCP can result in storage of the drug in various compartments in the body and influence the course of an acute overdose. This may account for certain variations in data seen among patients. The cursory application of our emerging concept of treatment (Aronow and Done 1978) to one patient with a history of chronic use resulted in at least an initial improvement. This has led us to undertake further studies of such cases.

ACKNOWLEDGMENTS

The authors wish to acknowledge the invaluable contributions of Dr. Annette Kelly of Henry Ford Hospital, Dr. Lynn Van Wagnen, Dr. Larry Fleischmann, Dr. Edgardo Arcinue, Dr. Ashok Samaik, David Ryan and the personnel of the Intensive Care Unit, Children's Hospital of Michigan.

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Chapter 13

The Diagnosis and Treatment of the PCP Abuse Syndrome

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INTRODUCTION

Our first exposure to PCP occurred during the summer of 1967 in the Haight-Ashbury District of San Francisco in which the drug was first introduced as the "PeaCe Pill" during a rock concert. We saw that day between twenty-five and thirty acute PCP toxic reactions. In some respects, these reactions were like the bad LSD trips we were used to treating, but in other respects quite different, with greater physical toxicity and paranoid thinking. We had samples of the "PeaCe Pill" analyzed through a local Bay Area toxicology laboratory and found that the psychoactive drug was PCP. The "PeaCe Pill" was not well received by the majority of individuals in Haight-Ashbury at that time, although PCP became the drug of choice for a small number of users who continued to use it on a chronic basis. For them most part, PCP was a drug of deception, usually marketed as "THC" or as one of the psychedelics which were more in demand. Within the past five years, however, PCP has become increasingly visible as a primary drug of abuse under a variety of street names, including "hog," "krystal," and "angel's dust." The drug is illicitly manufactured and taken in a variety of ways: orally, intranasally, and by intramuscular or intravenous injection. This paper provides the clinician who treats PCP problem with a conceptual framework for the diagnosis and treatment of the PCP abuse syndrome. Certainly not everybody who uses PCP develops toxic consequences, but we have seen a variety of short term and long term adverse reactions and have found that many clinicians have difficulty in both the diagnosis and treatment of PCP-induced problems. (Our work is based primarily on the following clinical experience: 1) the Haight-Ashbury Free Medical Clinic Drug Detoxification and Aftercare Program; 2) our Emergency Medical Service at rock concerts; 3) Patient consultation through our Physician Training and Consultation gram, in which we receive telephone calls and individual requests from physicians treating people who have PCP abuse problems; 4) Outreach Training and Clinical Work: 5) Inpatient treatment of PCP abusers at Gladman Psychiatric Hospital: 6) our collective private practices; 7) work and patient consultation with other community based treatment agencies; and 8) fellow clinical investigators. Our information is based on our clinical experience and review of literature. There are many more questions than there are answers, and the clinical staging presented later in this paper is designed primarily for the clinician, not the PCP researcher. As the PCP abuse problem has increased, clinicians all over the country are faced with management of various stages of PCP abuse with relatively little help on diagnosis and treatment.

The effects observed when PCP is ingested result from a complex interaction among pharmacological, physical, and sociocultural variables, and the pre-PCP psychological makeup of the individual. In the natural setting, of course, these variables cannot be isolated. In designing the diagnostic and treatment plan, one is confronted with their simultaneous interaction.

Our clinical findings show four behavioral phases of the PCP abuse syndrome, which may appear as successive stages.

Stage I. Acute PCP toxicity: These reactions are a direct result of PCP intoxication. Their onset may be minutes to hours following PCP ingestion.

Stage II. PCP toxic psychosis: This stage is apparently not related to toxic blood levels of PCP and does not inevitably follow stage I.

Stage III. PCP-precipitated psychotic episodes: In some individuals, PCP may precipitate a psychotic reaction lasting a month or more which clinically appears much like schizophrenia.

Stage IV. PCP-induced depression: PCP can produce a depressive reaction in some individuals. This may follow any of the previous stages and last from one day to several months.

Each stage is shown in outline in table I and will be described in more detail, followed by case histories illustrating salient clinical features.

DISCUSSION AND CASE HISTORIES

STAGE I. ACUTE PCP TOXICITY

In acute PCP toxicity there are four "C's": combativeness, catatonia, convulsions and coma. These effects are dose-related. Combativeness and catatonia are frequently observed together at the lower dosages, while convulsions and coma are related to higher dosage effects. During this stage, one also sees hypertensive crisis sufficiently severe to be fatal, although such crises are relatively rare in our experience. Illusions can dominate: space walking, the detachment of sounds, objects changing in size, shape, and distance. Visual illusions rather than true

TABLE 1

DIAGNOSIS AND TREATMENT OF THE PCP ABUSE SYNDROME

Patient	Age (Yrs/Mos)	Weight (Kg)	Serum PCP, ng/ml (interval post-ingestion) at admission[a]	peak measured	Clinical Manifestations	Duration (from time of ingestion	Treatment[b] (time from admission)
5	18/11	59	66	138	coma	10.3 da	Tracheal intubation
			(9 da)	(10.1 da)	restless	10.7 da	1.9 d
					semicomatose	11.0 da	Gastric drainage
					disoriented	12.8 da	NH_4CL
					sleepy	15.5 da	Ascorbic Acid
					EEG abnormal:		Diazepam x 2 d 8
					delta rhythm	5.0 da	Furosemide, 25 mg
					dysrhythmia	1.0 da	x 6 d .9, 1.2, 2.0,
							2.7, 3.3, 6
6	15/8	58	280				
			(1.3 da)	Same	coma	2.4 da	Gastric drainage
					hypertonus	2.3 da	NH_4CL
					semicomatose	2.8 da	Ascorbic acid
					disoriented	4.6 da	Furosemide, 65 mg,
					excessive sleep	5.0 da	27 mg x 2 d 1
					EEG abnormal:		
					delta rhythm	5.0 da	
					dysrhythmia	8+da	
7	16/3	60	221	Same	convulsions	2 hr	Gastric drainage
			(0.8 da)		apnea spells	12 hr	NH_4CL
					coma	1.25 da	Ascorbic acid
					agitat., ↑tonus	1.25 da	Histalog, 50 mg,
					disorientation	3 da	x 1 d 1.25
					excessive sleep	7 da	Furosemide, 35 mg
							x 3 d 1.75, 2.5, 3.8
8	17/10	60	2.7	5.1	mania, disoriented		Gastric drainage
				(unknown[d])	hyperacusis		NH_4CL, Ascorbic acid
					compulsive talking		Furosemide x 4

[a]Children's Hospital of Michigan [c]Followed at another hospital [d]Chronic ingestion

[b]In addition to the supportive care, gastric lavage and IV fluids given to all eight

hallucinations are common, but occasionally auditory hallucinations occur. If the dose of PCP is high enough, the patient may have many grand mal seizures and coma which require hospitalization and supportive care to stabilize and maintain the respiratory and cardiovascular function. With proper management, most patients who go into a PCP-induced coma survive, although the period of coma may be quite prolonged. Our experience indicates that the usual duration of acute PCP toxicity is 0 to 72 hours. Lab results indicate that blood is almost always positive and urine is positive. A large number of people clear after stage I, PCP acute toxicity; some go into stage II, PCP toxic psychosis.

Case 1

At a rock concert in the San Francisco Bay Area, six adolescents who had previously experimented with a variety of psychoactive drugs, including PCP, ingested an unknown quantity of PCP in tablet form. Although they had experience with PCP, they had been primarily smoking it in a form of "krystal joints," and this was their first exposure to the tablet form of PCP. All six became acutely intoxicated; one, a 17-year-old white male high school senior, became comatose. Friends took him to the emergency room of a local hospital after observing the young man for a couple of hours and becoming concerned over his extreme muscular rigidity and shallow respirations. He was hospitalized and maintained on a respirator for over three days. With this supportive management he recovered fully, but there was a period of cerebral dysfunction with poor memory and depression lasting for over a week following the acute PCP toxicity. This case example also demonstrates that a patient can go from stage I acute PCP toxicity to stage IV, cerebral dysfunction and depression, without going through stage II and stage III psychotic phases.

Treatment of Stage I

Acute PCP toxicity patients can be divided into two groups: those who are comatose, and those who are acutely intoxicated but conscious.

A. Comatose Patients

As in the management of any coma patient, the first level of consideration is stabilization of the ventilation and cardiovascular systems, and protecting the individual from inflicting bodily harm. Secondly, consideration should be given to the elimination of the offending agent.

1. Stabilization of medical signs and psychiatric signs and symptoms.

a. Cardiovascular System

Treatment of the hypertension with Hyperstat has been recommended (Eastman and Cohen 1975).

b. Convulsions

Convulsions may occur and are not necessarily limited to one or two. Therefore, treatment is recommended with intravenous diazepam (Valium[R]) given over a period of two minutes following the seizure.

c. Respiratory Depression

Respiratory depression with pure PCP is unusual except in very high dosages. However, respiratory depression may be marked when combined with alcohol, other sedative hypnotics, or opiates. If the patient is sufficiently depressed, respiratory assistance on a respirator is necessary.

B. Conscious Patients

Patients in acute toxicity may also present as psychiatric emergencies with symptoms of paranoia, agitation, thought disorder, negativism, hostility, and grossly altered body image. Assaultive and antisocial behavior often results in the individual's coming to the attention of treatment personnel. In the management of such individuals, Luisada and Brown (1976) have delineated the immediate goals of treatment as: 1) prevention of injury to the patient or others; 2) assurance of continuing treatment; 3) reduction of stimuli; 4) amelioration of the psychosis: and 5) the reduction of agitation. The reduction of external stimulation through the use of seclusion or a "quiet room" is of prime importance. Clinicians disagree as to the most appropriate pharmacological intervention. Luisada and Brown (1976) recommend chlorpromazine (Thorazine), although we generally prefer diazepam (Valium) for symptomatic or behavioral control. Haloperidol (Haldol) has also been used (Showalter and Thornton 1977).

C. Elimination of PCP from the body

Although many clinicians prefer conservative supportive management, Aronow, Miceli, and Done (this volume) have successfully utilized continuous gastric suction, acidification of the urine, and a potent diuretic such as furosemide (Lasix) to enhance elimination of the PCP. Their technique and rationale for use are described in detail in other papers in this volume. PCP is recycled through the enterohepatic circulation, and introducing a slurry of activated charcoal into the intestine may decrease reabsorption of PCP from the small intestine. This should <u>not</u> be used instead of gastric suction in a comatose patient; however, 100 ml of activated charcoal slurry should be inserted into the stomach just before the nasogastric tube is removed, or may be given orally to a noncomatose patient.

STAGE II. PCP TOXIC PSYCHOSIS

After the acute PCP toxicity phase has passed, some individuals develop a prolonged toxic psychosis. Our experience has been that incidence of the PCP toxic psychosis is highest among chronic abusers. In trying to detemine prognostic indicators to why certain patients will become psychotic, we have looked at different clinical variables, but found chronic abuse to be the major factor. In this stage, one finds impaired judgment and paranoid delusions with agitation and both auditory and visual hallucinations. The individual can be self-destructive or destructive to others. Hallucinations and flattened affect are characteristic. The usual duration is 24 hours to 7 days or more. Lab results indicate blood negative and urine positive for PCP. The amount of PCP excreted in the urine is highly dependent upon urinary acidity, and an attempt to collect the urine under conditions of urinary acidification with ammonium chloride or ascorbic acid (vitamin C) should be made.

Case 2

A 38-year-old black male with no previous history of drug abuse or psychiatric problem acquired some new marihuana which was described to him as "superweed." He had regularly smoked marihuana for over twenty years and described no adverse consequences of any sort with its use. He began smoking this new "superweed" and found himself (according to his girlfriend) beaming paranoid, delusional, and uncharacteristically hostile. After approximately two weeks of daily smoking of the "superweed" he felt that there might be some correlation between this new drug and his symptoms and stopped smoking the drug for a day. He found no symptom relief; after that, he actually increased the dosage, as he felt it might help him feel better and recover from the symptoms which he felt were unrelated to the drug use. Shortly after, he became quite assaultive, cut off the head of his dog, and assaulted a stranger on the street with a razor. His girlfriend, who had read in the newspaper of the bizarre behavior PCP can produce, brought him to the Haight-Ashbury Free Medical Clinic where he was examined. The material was analyzed and found to be marihuana laced with a significant quantity of PCP. The toxicity of PCP was explained to both the patient and his girlfriend. Both decided on an abrupt cessation of the drug. Following a brief period of hospitalization in which antipsychotic medication was administered, the patient was discharged and refused further hospitalization or medication, but remained in supportive counseling. After approximately two weeks the psychotic symptomatology faded, but the patient still complained of impaired thinking, difficulty in believing that the delusions that he perceived during his PCP intoxication were unreal, and prolonged depression. Weekly supportive counseling without medication gradually resolved these symptoms in approximately twelve weeks.

Treatment of Stage II

Most clinicians recommend the use of non-phenothiazine tranquilizers such as haloperidol (Haldol). Some clinicians use sedative hypnotic medication. There is no sound research basis for the use of either of these medications; nor in our experience, is there any indication that these medications shorten the course of acute PCP toxic psychosis. It does appear, however, that they make the patient more manageable in a ward, which is probably the major reason that these medications are used. In those clinical cases that we have seen where patients have received either no medication, sedative hypnotic medication, or antipsychotic medication, these variables do not appear to change the total length of time the individual is psychotic, but they do modify the characteristic symptoms.

STAGE III. PCP-PRECIPITATED PSYCHOTIC EPISODE

Early investigators reported on the tendency of PCP to exaggerate signs and symptoms in schizophrenic patients (Luby et al. 1959, and Domino 1964). Many other studies have described the PCP-induced psychosis. Luisada and Brown (1976) have described individuals who were not previously schizophrenic, who became so following ingestion of PCP, and who periodically have return of symptoms, although of less intense nature than when the PCP was first used. To what extent it is possible to have a prolonged psychosis in an individual who is not predisposed to schizophrenia is not known. Certain individuals, mostly with psychotic or prepsychotic personalities, tend to develop a PCP-precipitated psychotic episode that mimics schizophrenia. This may occur after a single dose administration of PCP. This is not a result of chronic PCP abuse producing a toxic psychosis, but rather a PCP-precipitated adverse reaction to an underlying psychological condition. The characteristics of the episode are of the schizo-affective type with paranoid features and a waxing and waning thought disorder, A majority of the cases that we have seen in stage III have had psychotic or prepsychotic personalities, and we believe that this is the major prognostic indicator. However, we have seen a few cases that have had a prolonged PCP-precipitated psychotic episode after single dose administration, with no unequivocal history of preexisting psychosis. Our time range is 7 days to 30 days or more, with patients moving from the PCP toxic psychosis into the PCP-precipitated psychotic episode. Lab results indicate blood negative, urine negative. Most investigators recommend the use of chlorpromazine (Thorazine) in dosages comparable to those used in schizophrenia and remark that the paranoia appears to yield at a slower rate (Luisada et al. 1976). The need for long term antipsychotic drug maintenance for the individual with PCP-precipitated psychotic episodes makes it important to differentiate the PCP-induced toxic psychosis from the PCP-precipitated psychosis. It is also important to emphasize that individuals with schizophrenia can go into a prolonged psychotic phase after a single dose of PCP. This is demonstrated by the following case:

Case 3

A 26-year-old white female with a long history of psychiatric disturbance, including hospitalization for psychosis, but no history of alcohol or drug abuse, was at a party and shared a joint of "angel dust," a drug with which she had no previous experience. After smoking approximately half of the joint, she started becoming quite paranoid and delusional, and developed both auditory and visual hallucinations. After remaining at home with her parents for two days, she was taken to a San Francisco psychiatric hospital where she was admitted. The material she smoked was analyzed and found to contain PCP. At the time of hospitalization, both her blood and urine were negative for PCP. She remained psychotic for over two weeks, but the thought disorder gradually faded, giving way to a substantial depression. Her psychosis was treated with haloperidol (Haldol).

Treatment of Stage III

A. Immediate goals of treatment are the same as those described for acute PCP toxicity, including prevention of injury and reduction of stimuli.

During the PCP-related psychotic break, it appears that the drug precipitates an underlying thought disorder, rather than producing a direct toxic psychosis, which we define as a major break with reality secondary to an intoxicant. In general, many clinicians use a non-phenothiazine major traquilizer, such as haloperidol (Haldol), for the PCP toxic psychosis because of the concern over the additive effect between PCP arid chlorpromazine (Thorazine). However, there is no controlled research in humans to support this. Domino and Luby (1972) have described animal research which shows some additive effect of chlorpromazine (Thorazine) and PCP. In PCP-precipitated psychosis, however, experienced clinicians (Luisada and Reddick 1975) recommend residential seclusion with frequent observation and high doses of antipsychotic phenothiazine medication, such as chlorpromazine (Thorazine) given daily, starting with 400 mg a day in divided doses and increased as necessary by 200 mg a day to an average daily dose of 1600 mg per day. Clinical experience in the San Francisco Bay Area has varied between the use of sedative hypnotic medication such as diazepam (Valium) and low doses of haloperidol (Haldol) and has avoided the high doses of chlorpromazine (Thorazine) as described by Luisada and Reddick (1978). All clinicians treating stage III, however, agree that the PCP-induced psychotic reaction can be quite prolonged and should be managed on an inpatient basis.

STAGE IV. PCP-INDUCED DEPRESSION

PCP-induced depressionis a very frequent condition that many clinicians miss, particularly when it comes after a stage III PCP-precipitated psychotic reaction. The clinician is so relieved when the psychosis is over that s/he discharges the patient with relatively little followup and without realizing that in this depression the individual has high suicide liability or may use other types of drugs to alleviate the depression. A paradox with PCP is that it does give an energizing, numbing, consciousness-altering effect which the patient perceives as antidepressant.

Clinically, it appears that many of these patients have prolonged cerebral dysfunction, as well as depression. The complaints of memory impairment subside as the depression clears. The patients who we have treated have indicated that they feel less depressed as they think their "brain damage" is clearing. It becomes very difficult to figure out whether depression clears as the cerebral dysfunction itself clears or as their concern over the cerebral dysfunction waves. In addition, some of the symptoms may be the result of the depression rather than the cause. PCP-induced depression can last from one day to several months, and can follow any of the preceding stages. That is to say, the patient can be in PCP acute toxicity and clear with no problem, or go into stage II PCP toxic psychosis, or into stage III PCP-precipitated psychotic espisode, and then have prolonged PCP-induced depression. Or, the patient can wake up from a PCP acute toxic reaction and go right into the prolonged depression. Laboratory results will show blood and urine both negative for PCP.

Case 4

A 19-year-old white female came to the Haight-Ashbury Free Medical Clinic after a PCP overdose. She described a long history of agitated depression and suicidal ideation from which she found she gained relief when she "snorted" two lines of PCP containing approximately 20 mg each day. She indicated that drugs such as amphetamines actually made the depression worse because they increased the agitation. Conversely, when she took PCP, the alteration in consciousness and energizing effect gave her relief from the depression. When she stopped the PCP, however, she found the depression became worse than it was prior to use of the drug. She indicated that she had no intention of stopping prior to this me overdose episode. She expressed amazement about the overdose because she indicated that she had not snorted a higher dose on the day she became comatose.

This case illustrates a number of principles, including motivation for usage in individuals who are self-medicating their depression. In addition, it demonstrates that chronic abusers can have overdose episodes even if the dosage of the drug is not increased, and it suggests clinically that this may be the result of accumulation of the drug in both brain and fatty tissues of the body. Also, there is a high incidence of secondary drug abuse following this stage IV PCP-induced depression. Many individuals turn to other drugs, including alcohol, stimulants such as amphetamines or cocaine, or even heroin to deal with the PCP-induced depression. This is illustrated by the following case:

Case 5

A 34-year-old white male used PCP by the intranasal route on a daily basis for three years. He developed a grandiose religious delusion in which he described himself as the "Prince of Peace" and thought he was "Jesus Christ." He was using PCP with a number of other friends, who also felt he was "Jesus." Following an adverse PCP reaction and confrontation with another individual using PCP, this religious delusion was shattered and he became extremely depressed. In an attempt to self-medicate this depression, he began snorting and finally injecting heroin and eventually became dependent on heroin. He also used large quantities of cocaine. As a consequence of antisocial activities undertaken in order to acquire the drug, he was arrested and served time in jail. He is how drug-free and involved in treatment in a non-medical outpatient program stressing a chemical-free philosophy. He denies that he had any history of depression prior to his prolonged period of PCP abuse, or any history of religious delusion. He feels that the depression and religious delusions were a direct result of his daily and prolonged abuse of PCP.

Treatment of Stage IV

We have not had notable success in treating PCP-induced depression with the tricyclic antidepressants amitriptyline (Elavil) and imipramine (Tofranil). Certainly, the PCP depression can result in return to PCP usage, or to a suicidal attempt for individuals who are self-medicating a preexisting depression with PCP. If treatment is initiated with antidepressants, full therapeutic dosages should be given 100 to 250 mg/day). Many of these patients take medication erratically, and the usual precautions used with patients on tricyclic antidepressants should be observed. We certainly prefer inpatient treatment. If antidepressants are prescribed on an outpatient basis, not more than two or three days' dosages should be dispensed at once. The patient should be cautioned about possible interaction of tricyclic antidepressants with PCP, alcohol, and other drugs, and advised to discontinue the tricyclic antidepressants if PCP usage is resumed. The underlying basis of a PCP-induced depression is unknown, and no controlled clinical procedures are available to guide the clinician.

SUMMARY AND QUESTIONS FOR FUTURE RESEARCH

PCP abuse may present in a variety of ways to the clinician. Treatment strategies may be conceptualized in terms of four stages, each having specific types of treatment intervention: acute PCP toxicity: PCP toxic psychosis; PCP-precipitated psychosis; and PCP-induced depression. Clinical treatment of the severe overdose in coma is best understood and defined by clinical protocol. The treatment of other stages is still primarily dictated by clinical intuition; disagreement exists among experienced clinicians as to what constitutes the most appropriate treatment.

For the clinician responsible for treating PCP abuse, a number of Clinically important questions remain unanswered. For example:

1. Does chronic PCP use produce long-lasting, perhaps permanent, brain damage? Is the association observed by clinicians spurious in that most PCP users have used a variety of other drugs? Are the effects thought to be long term actually secondary to

chronic intoxication?

2. Does PCP ingestion produce long-lasting psychological disorganization in individuals who are not schizophrenic? If so, how can these effects be characterized and distinguished from schizophrenia?

3. Are the antipsychotics useful in shortening the duration or intensity of PCP acute toxicity, the PCP toxic psychosis, or the PCP-precipitated psychosis? Should patients who manifest prolonged psychoses following PCP ingestion be diagnosed or treated differently than schizophrenics?

4. Is the PCP-induced depression observed in PCP users actually induced by the drug? If so, what is the underlying biochemical mechanism, and should the antidepressants be used in treatment of the depression?

The answers to these and other clinically relevant questions can be resolved by careful clinical research. In view of the current differing opinions as treatment, double blind random treatment assignment studies should be undertaken. Practically, the barriers to definitive research include the difficulty in establishing informed consent to participate in a study while the patient is acutely psychotic and the difficulties inherent funding such research. Until answers are available, prudent clinical treatment must proceed according to clinical intuition. We believe the concept of distinct clinical stages is a step toward rational treatment.

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Chapter 14

The Phencyclidine Psychosis: Phenomenology and Treatment

Paul V. Luisada, M.D.

INTRODUCTION

Washington, D.C. has been a major center for phencyclidine (PCP) production and abuse since the early 1970's. This phenomenon, however, did not reach the awareness of the public or of most mental health professionals until mid-1977.

Phencyclidine's propensity for reactivating schizophrenic psychoses also remained buried in the literature on model psychoses from the early 1960's. Finally, the fact that phencyclidine can produce long-term treatment-resistant schizophreniform psychoses in subjects who have had no prior psychiatric histories was not known until 1974. This paper concerns itself with the diagnosis and clinical management of the phencyclidine psychosis.

During the fall of 1973, the admission rate for what appeared to be unusually long, severe, and treatment-resistant initial schizophrenic psychoses suddenly tripled at the Area D Community Mental Health Center in Washington, D.C. (Luisada and Reddick 1975). These patients had all smoked a drug called "Angel Dust" before becoming psychotic. Unlike the vast majority of toxic psychoses, however, these episodes often required two weeks of aggressive inpatient treatment before resolution began. In addition, violently agressive behavior was characteristic of the onset, and the presenting picture was at first indistinguishable from a florid schizophrenic episode.

The first case to catch our attention was unusual in several ways and presented a diagnostic dilemma: An 18-year-old high school senior was admitted after becoming violently psychotic at home without any prodromal signs. He presented with the primary and secondary signs of a florid schizophrenic psychosis. Escalating doses of major tranquillizers and intensive staff involvement failed to influence his illness during the first two weeks in the hospital. In fact, contact with staff appeared to aggravate his symptoms. His ambivalence and paranoia made him unpredictable and posed a constant threat of violence. He assumed bizarre autistic postures, demonstrated a formal thought disorder, and voiced the delusions that his mother was dead and that he had a "knot" in his head.

The diagnosis was complicated by several factors: his mother denied a family history of schizophrenia or the presence of prodromal signs and symptoms in the patient. A toxic psychosis seemed improbable on the basis of lack of history or physical stigmata, the absence of a clouded sensorium, the persistence of the psychosis, and the presence of all four primary signs of schizophrenia.

When the patient's personality was dramatically reconstituted to its premorbid level in the third and fourth weeks of hospitalization, however, he reported smoking a drug called "angel dust" just prior to admission.

Similar admissions rose from a trickle to a flood, peaking in February 1974 at the rate of one third of the first inpatient admissions. The epidemic ended even more suddenly, with no more than three cases each during April, May, and June. This decline followed by several weeks a police raid on local PCP laboratory.

Another epidemic began toward the end of 1974, and for some periods of 1975 and 1976 PCP psychosis became our leading cause of inpatient psychiatric admissions, surpassing both schizophrenia and alcoholism. By the beginning of 1976, the Drug Enforcement Administration was calling the Washington Metropolitan Area the PCP capital of the country. However, despite a proliferation of local laboratories (and an increase in raids on these laboratories), admissions to our center for PCP psychosis began a slow but steady decline. At the same time, experienced drug users presenting for treatment of other drug abuse problem began referring to PCP as a drug to avoid "because it makes people crazy." Meanwhile, the suburbs began experiencing noticeable increases in the incidence of PCP psychoses.

PCP presently remains the major drug of abuse in the Washington Metropolitan Area. This situation prevails despite a recent wave of local media publicity about its adverse effects.

DEFINITION

The PCP psychosis may be defined as a schizophreniform psychosis which occurs in some individuals after phencyclidine use and which persists for more than a day. The psychosis may last for days or weeks despite abstinence, and it characteristically becomes more severe during the first few days of its course.

The PCP psychosis is characterized by the appearance of the cardinal signs of schizophrenia and unpredictable aggressive or withdrawn behavior. Characteristically, there is autistic and delusional thinking, commonly including global paranoia, delusions of superhuman strength and invulnerability, as well as delusions of persecution and grandiosity. A formal thought disorder, with loosening of associations, blocking and auditory hallucinations can be demonstrated. Affect is generally blunted, with periods of suspiciousness often alternating with extreme anger or terror. Patients are ambivalent and unpredictable even toward their close friends and relatives.

Behavior is extremely unpredictable. These patients may be reluctantly cooperative one minute and violently assaultive the next. Some carry lethal weapons to protect themselves from their imagined persecutors. Bystanders have often been furiously, unexpectedly, and unremittingly attacked without provocation, because the psychosis may include both extreme global paranoia and delusions of superhuman strength.

REVIEW

PCP was originally developed in the 1940's by Parke, Davis & Co. as an intravenous general anesthetic under the trade name "Sernyl." Animal trials demonstrated very high levels of general anesthesia (Chen et al. 1959). Lower doses produced a cataleptic state, and still lower doses a tranquilized state during which fingers could be inserted in wild animals' mouths with impunity (Davies and Beech 1960). PCP was later used to tranquilize wild animals for handling (Domino 1964), and it is still available for veterinary use (Reed and Kane 1972).

Initial trials with humans were undertaken with the expectation that PCP would have great promise for surgical anesthesia. As an anesthetic, it fulfilled all expectations until the patients woke up: one-sixth of the original group were severely psychotic, but only for several hours. Their behavior was described as extremely agitated and bizarre, with echolalia and logorrhea as prominent symptoms (Greifenstein et al. 1958). Significantly, this psychotic reaction was most common in young or middle aged males (Johnstone 1960).

Because of these severe postoperative reactions, the focus of investigation of PCP in humans shifted from its possible use as an anesthetic to its utility for producing model psychoses. The drug was given to "normal volunteers" whose psychoses were documented in an eruption of papers which lasted until 1965, when Parke-Davis withdrew PCP from experimental use in humans (Reed and Kane 1972).

The major finding of these studies was that PCP had no equal in its ability to produce brief psychoses nearly indistinguishable from schizophrenia (Rosenbaum et al. 1959). Generally, the psychoses began immediately after infusion of the drug (Davies and Beech 1960), lasted about two hours, and were characterized by changes in body-image, thought disorders, estrangement, autism, and occasional catatonia (Luby et al 1959). Subjects reported feeling numb, had great difficulty differentiating between themselves and their surroundings, and complained afterward of feeling extremely isolated and apathetic (Bakker and Amini 1961). Of particular interest was the observation that these volunteers often became violently paranoid while acutely psychotic.

Other workers who compared PCP is mescaline and LSD commented on the ego-alien quality of the psychoses (Dan et al. 1961). Pre-occupation with death and fear of death was common while under the influence of the drug, and it had an impressive ability to loosen up these subjects! unconscious conflicts.

Although these studies agreed that PCP can produce schizophrenia on demand in "normal volunteers," the psychoses were limited to a maximum of several hours. By contrast, when Luby gave PCP to four hospitalized chronic schizophrenics, the results were much more severe (Luby et al. 1959). "It was as though in these patients, the acute phase of their illness had been reinstated." They became nearly unmanageable in an inpatient setting, not for several hours, but for six weeks. Other observers noted that PCP's effects on schizophrenics are exactly the opposite of LSD's, since schizophrenics are considerably more resistant than "normals" to that drug.

The literature on PCP in humans therefore describes two related but distinct psychotic effects:

- A schizophrenic syndrome lasting several hours in "normals."
- An extreme exacerbation of their psychoses lasting up to 6 weeks in chronic schizophrenics.

The psychoses we have seen seem to fall between these categories. Although our patients had not been hospitalized before, lacked prior psychiatric histories, and were living in the community, their psychoses were longer and more severe than those described in "normal volunteers," but shorter than those described in schizophrenics: yet they seemed to resolve without sequelae.

METHOD

To describe the clinical aspects of this syndrome more precisely, we selected for study a group of PCP users in the following way: We screened the 200 inpatient admissions to a single catchment admission ward in the CMHC between July 1973 and June 1974, which approximated the epidemic's time-frame. The records of all patients who were psychotic on admission or had a history of drug use were examined for an explicit history of exclusive PCP use during the two months before admission. After applying these selection criteria, we were left with 11 men.

These selection criteria resulted in the exclusion of about two-thirds of PCP-related admissions. These exclusions were all on the basis of multiple drug-use, and were made in order to limit the drug effects to those of PCP as much as possible. The following observations were assembled from the patients' charts, nursing notes, ward logs, and shift reports.

CLINICAL COURSE

The course of the treated psychosis was found to consist of three distinguishable phases of approximately equal length over the course of an average two-week hospitalization: The initial phase is characterized by the violent, psychotic behavior described earlier, and this persists for an average of five days. During the second phase, behavior is more controlled, but patients remain restless and unpredictable for approximately five more days. The final phase lasts about four days and is characterized by rapid personality reintegration and rapid disappearance of thought disorders and paranoia.

The majority of patients presenting with this entity were in their late teens to mid-twenties, and the majority have been males. most did not reach treatment until hours or days after the onset of the psychosos, and did so during its initial phase. Chief complaints ranged from mute posturing to "attacking everyone in sight." The majority of these patients were brought to treatment after their aggressive behavior exceded the limits tolerated by family, friends and police. Those few patients who presented themselves voluntarily were generally treatable on the outpatient basis, and were neither as violent, as agitated, nor as psychotic as those described here.

Where admission histories were obtained from these patients, they generally included several days of confusion, paranoid ideation, insomnia, and intermittent restlessness. However, a history of phencyclidine use was not reliably obtainable on admission, and some of the patients were initially misdiagnosed as schizophrenic. Family numbers generally describe the pre-admission period as characterized by continuous insomnia, tension, hyperactivity, and intermittent, unexpected aggressive behavior, bizarre paranoid delusions, ideas of reference, delusions of being controlled by others, and grandiosity, but no fixed or systematized delusional system.

Apart from the characteristic history of acute onset, and an irregularly obtained history of using PCP in its current street guises, the majority of these patients lacked prior psychiatric histories and tended to be more independent of their families than schizophrenics. Most were doing reasonably well in high school, college, or work, although some did have poorer social adjustments prior to the onset of their psychoses.

Other patients we have seen had prior admissions for schizophrenia but experienced sudden psychotic reactivations after experimenting with PCP. As a rule, these psychoses involved significantly more violent and unpredictable behavior than the initial schizophrenic psychoses.

CLINICAL MANAGEMENT

Phencyclidine psychosis in the initial phase constitutes a psychiatric emergency; hence, its early, acurate diagnosis is of great importance. These patients are an immediate danger to others merely on the basis of their misperceptions, paranoia and hostility; and this threat is compounded by their confusion, tendency toward violence, and the extreme unpredictability of their behavior. They also constitute a danger to themselves not only on the basis of impaired judgment and inability to care for themselves, but also because their violent, threatening behavior may provoke lethal countermeasure by those around them. Burns has reported a case of PCP intoxication in which the patient was shot and killed by police after not heeding their warnings. One of our patients was hospitalized involuntarily on the basis of "attacking everyone in sight," including the investigating police officer, after a car accident.

Patients in the initial stages of the PCP psychosis almost invariably require inpatient psychiatric treatment. Furthermore, these patients are poor candidates for voluntary treatment, first because their paranoia makes them unlikely to sign on admission, and second because their restlessness, ambivalence, confusion, and unpredictability at this stage of the psychosis lead to a high percentage of premature discharges against medical advice. A factor which further militates against successfully continuing treatment on a voluntary basis is admission under pressure from family or friends. These patients often demand to leave as soon as their relatives and friends return home. In our experience, they cannot be dissuaded on the basis of rational discussion during this phase of their illness. In one instance, a newly admitted patient insisted on "fighting my way out" despite the presence of sixteen male nursing staff, some of whom were injured in the process of restraining him.

As discussed above, patients in the initial stage of the PCP psychosis are dangerous, ambivalent, unpredictable, psychotic and agitated. The immediate goals of treatment are therefore:

(1) Prevention of injury to the patient or others
(2) Assurance of continuing treatment
(3) Reduction of stimuli
(4) Amelioration of the psychosis
(5) Reduction of agitation

Treatment which meets the first three of these goals included prompt inpatient hospitalization, preferably on an involuntary Isolation in a bare, locked seclusion room with frequent but unobtrusive observation is the treatment of choice. Seclusion not only safegards other patients and staff but also calms the patient through the reduction of stimuli which he can misperceive as threatening. This applies particularly to the sight of other people.

Chlorpromazine is the only antipsychotic agent which meets the last two goals: amelioration of the psychosis and sedation. Our experience indicates that the use of nonsedating antipsychotic agents prolongs the time these patients require seclusion, delays improvement of the insomnia, and makes them more difficult for staff to manage at mealtimes. Although the use of sedatives such as diazepam and chlordiazepoxide has been suggested for the management of acute phencyclidine intoxication, the dual treatment goals of ameliorating the psychosis and reducing agitation make the use of a single drug which meets both goals (chlorpromazine) more attractive than the combination of a nonsedating antipsychotic agent and a sedative.

Some authors have noted that chlorpromazine has not been shown to antagonize the behavioral effects of PCP, and even enhances some of then (Balster and Chait 1976). These conclusions, however, are based upon observations of animals intoxicated with PCP who were given chlorpromazine. There is some doubt as to whether these conclusions apply to the PCP psychosis as seen in humans. First, behavioral changes persisting for days or weeks after PCP intoxication have been reported only in humans. Thus there is no animal model for the PCP psychosis. Second, the experiments were performed chiefly on monkeys, and PCP's effects on monkeys is tranquilization, not the psychotic agitation seen in humans. Finally, chlorpromazine enhances the depressant effect of PCP on these animals. Our experience has been that chlorpromazine also acts as a depressant in our patients, and that it antagonizes the persistent excited behavior seen in humans with the PCP psychosis.

Once the possibility of anticholinergic drug intoxication has been ruled out, the daily dose of chlorpromazine is increased by 200 to 400 milligrams per day from a starting dose of 400 milligrams per day in divided doses. On the average, a daily dose of 1600 milligrams per day has been reached by the end of the initial phase of the psychosis.

Behavior in seclusion during the initial phase is characterized by continuing global paranoia, insomnia, anorexia, intermittent agitation, and strong reactions to such stimuli as the presence of staff during meal times. Patients may throw food about the rooms or smear it on the walls. They are extremely suspicious of food and oral medication, and may vacillate at length before reluctantly accepting it. It is helpful if the same staff members bring the patient's food and medication from day to day.

This slow response to the most aggressive treatment is characteristic of the phencyclidine psychosis and sets it apart from paranoid schizophrenia, in which equally agitated patients respond much more rapidly. Indeed, the sense of lack of progress engendered by this slow treatment response was a factor leading to our first investigation of these psychoses.

The transition from the initial to the <u>mixed phase</u> is characterized by several gradual changes which become prominent around the fifth day of treatment: Although restless, the patient is no longer hyperactive: he is less threatened by or overtly hostile to the presence of others in the seclusion room. He is cooperative to the extent of following simple concrete suggestions, and accepts medication without suspicious vacillation. He can agree to seclude himself if he becomes upset.

Thus, although he is confused, still demonstrates a thought disorder, hallucinations, blocking, and paranoid ideation, he is relatively calm and reasonable a good portion of the time and can accept some degree of responsibility for and control of his behavior.

Despite these signs of progress, there are still intermittent periods of gross paranoia, agitation, terror, and hyperactivity alternating with quiet paranoid watchfulness. Affect remains quite constricted, and inappropriate demands which are not met immediately may explode in an unexpected flurry of violence. Thus, patients in the second (mixed) phase are psychotic, paranoid, unpredictable and intermittently dangerous, although they are no longer as sensitive to stimuli.

The goals of treatment in this stage are:

(1) Prevention of injury
(2) Amelioration of the psychosis
(3) Reduction of paranoia

The first goal may be met by close and continuous monitoring of behavior and a flexible seclusion policy aimed at helping the patient voluntarily to seek seclusion at the first signs that he is losing control. Operationally, a patient who sits near other patients shows stability, whereas a patient who isolates himself in a comer with his back to the wall, watching others suspiciously, requires further isolation.

Clinical judgmemt will indicate whether further increases in chlorpromazine dosage, or switching to an equipotent dose of a nonsedating antipsychotic agent is indicated. Reestablishment of sleep pattern may be aided by switching the entire dose to bedtime. Participation in group and milieu therapy is helpful in restoring the patient's confidence in his perceptions and in establishing rapport.

The <u>third phase</u> begins, on an average, during the tenth day of hospitalization, and is characterized by rapid reintegration of the premorbid personality and the development of insight into the events leading to the hospitalization. There is often some amnesia for the early events of the psychosis, but a history of the use of phencyclidine prior to its onset is usually obtained during this period. Patients may be converted to voluntary status during this stage, and the groundwork for outpatient followup laid.

Outpatient followup is helpful as patients are tapered off medication. In this connection, it is interesting to note that despite repeated warnings against further phencyclidine use, a large proportion of our patients use it at least one more time and return for treatment of a second psychotic episode. Most of these patients explained using the drug again on the basis of "feeling good" and wanting to see if they could "handle it."

Less encouraging is our finding that about one fourth of the patients originally treated for phencyclidine psychoses return within a year with schizophrenic psychoses in the absence of drug use. By contrast, these later episodes have lacked the characteristic violence of the phencyclidine-induced ones, and they have been much more quickly responsive to antipsychotic drugs; yet they have also left behind typical schizophrenic personality changes. Those patients who had experienced the longer phencyclidine psychoses were generally the same ones who returned later with schizophrenic ones.

Epidemics of drug abuse are nothing new in the United States. The past two decades have seen epidemics of heroin, LSD and several other drugs, while alcoholism has been endemic for centuries. Our experience with several epidemics of PCP psychosis, however, shows that widespread use of PCP in a community produces manifestations which are not only different, but also more dangerous in some ways.

As noted earlier, our epidemic of PCP psychoses did not initially seem related to drug abuse at all. Our community was experiencing what appeared to be an epidemic of schizophrenia. This was unusual only because the rate of new cases of schizophrenia in a given population does not fluctuate widely and because our community mental health center admits only patients who live in a specific part of the city. Even with our present hindsight, we cannot be certain about the exact time when patients with PCP psychoses began appearing at the doors of our center. Until we learned that those psychoses were drug-induced, these patients were diagnosed and treated as schizophrenic.

Our experience indicates that although PCP abuse is spreading to other parts of the country, its incidence, and particularly that of the PCP psychosis, tends to be under-reported for a number of reasons:

(1) The incidence of overdose, which is a common indicator of drug abuse patterns in a community, tends to be lower for PCP than the incidence of psychoses in areas where the drug is smoked rather than taken internally.

(2) As we have noted, the presenting symptoms of the PCP psychosis arc often indistinguishable from schizophrenia. This is compounded by the amnesia induced by PCP. Where it is possible to perform admission interviews on these patients, they usually do not recall taking the drug. Unless family or friends

are aware of the patient's drug use, no history is obtained and routine laboratory screens for drugs do not detect PCP. Consequently, these patients are reported as cases of schizophrenia, a label which may follow them for the rest of their lives.

(3) As Burns and others have reported (Burns et al. 1975), some PCP intoxications and psychoses result in violent or accidental deaths. In the absence of a routine toxicologic test for PCP, medical examiners may report such deaths as accidents rather than as the consequences of drug use.

The only signs that PCP abuse is prevalent in a community may be police seizures of the drug, an increase in violent and accidental deaths, and an increase in the number of new cases of "schizophrenia" admitted to mental hospitals. Unless public awareness of the dangers of PCP is raised, these statistics may never come together.

Another dimension of the PCP problem is the connection between the PCP psychosis and schizophrenia. The connection between schizophrenia and phencyclidine psychosis appears to go well beyond the phenomenological similarities. As reported by Luby, one of phencyclidine's unique qualities is not only to mimic schizophrenia, but also to reactivate schizophrenic psychoses. The treatment of phencyclidine psychoses outlined in this paper is also quite similar to that for extremely agitated schizophrenics. Furthermore, our experience indicates that people whose sensitivity to phencyclidine has been demonstrated by the development of a psychosis will develop another psychosis upon reexposure to the drug. Finally, there are some patients who have first experienced phencyclidine psychoses and later have developed schizophrenia.

The PCP psychoses seen in our patients approached those reported in chronic schizophrenics in terms of severity and duration: they were far more severe than those reported in 'normals" in term of both parameters. Yet none of the patients in our initial study had experienced prior schizophrenic psychoses, and most had been leading lives which demonstrated a fairly high level of social integration.

One interpretation of this apparent paradox might be that our patients literally do fall between the two groups reported in the literature in some way: Those PCP users in the catchment area with psychoses as brief as the ones experienced by "normal volunteers" would have improved before becoming inpatients and consequently would not have been admitted. All the hospitalized chronic schizophrenics in the catchment area were already on the CMHC's inpatient units and were therefore not exposed to the drug.

Our results support this interpretation, since they show a variation in the time required for recovery in our eleven patients which nearly spans the extremes reported in the literature. The patient with the briefest stay went through the three phases described earlier in about three days. The longest-hospitalized patient required about four weeks, and those in between tended to be evenly distributed. Furthermore, those patients who later returned and were rediagnosed as schizophrenics were at the upper end of the distribution in terms of the duration and severity of their psychoses. Thus, our study patients might represent that part of the population of the catchment area which is significantly more sensitive to PCP than "normals" but not so sensitive as chronic schizophrenics.

These findings suggest several further conclusions: First, they support those studies cited earlier which linked schizophrenia and sensitivity to PCP. Second, they suggest that sensitivity to the drug varies with the individual. Third, they suggest that this sensitivity, rather than being extreme for schizophrenics and mild for "normals," covers a wide sprectrum, with chronic schizophrenics at one extreme, and "normals" at the other: the patients studied here would therefore be distributed in between. Our "schizophrenia epidemic" might therefore be interpreted as evidence that the distinction between having or not having schizophrenia is not clearcut; perhaps it implies that in a large population, a graded continuum of "schizophrenia" exists between those who are most "schizophrenic" and those who are least so.

Thus, our experience with phencyclidine psychoses not only supports earlier finds that schizophrenics are highly sensitive to the drug, but also suggests the existence of an individual sensitivity to the drug, a sensitivity which is related to schizophrenia in some way. The widespread use of phencyclidine in our catchment area might even be viewed as a crude "screening test" for "schizophrenicity." The ease with which phencyclidine may be synthesized in large quantities on a clandestine bases raises the possibility that this "screening test" may soon spread elsewhere.

Finally, because PCP was so well-studied in its days as a promising anesthetic, we can offer some other more speculative correlations: Domino's research on monkeys with chronically implanted electrodes found that PCP had two major central effects which correlated with behavior: an enhancement of neocortical activity, and a nearly complete suppression of evoked potentials in the amygdala (Domino 1964). Delgado (1971) has found that electrical stimulation of this part of the limbic system in monkeys inhibits rage and enhances placidity. The studies suggest that an explanation for the high incidence of violent and aggressive behavior observed in our patients might include PCP's suppressant activity on the amygdala.

Domino's work also suggests a neurophysiological mechanism which might account for the persistence of our patients' psychoses long after the drug was presumably metabolized: He found that PCP selectively enhances the sensitivity of adrenergic and serotonergic neurons to their neurotransmitters, and that this enhancement persists long after the drug has been fully metabolized (Domino 1964). This explanation also supports recent studies implicating adrenergic and serotoninergic components of the limbic system in the mechanism of schizophrenia.

If there is a solution to the problem of PCP abuse, that solution is prevention. Practitioners must be alerted to the fact that PCP is not just another hallucinogen, to be warned about in the same breath as LSD. The public must be alerted to the fact that PCP is far more dangerous to some individuals than the other abused drugs. Medical examiners should consider toxicologic analysis for PCP in all deaths resulting from drowings, falls from high places, apparently avoidable accidents, and from attempts to contain violently assaultive subjects. Psychiatric facilities should investigate any sudden local increases in the incidence of schizophrenia, and should routinely include PCP psychosis in the differential diagnosis of all apparent schizophrenics in whom the illness is of acute onset and characterized by violent behavior, whether or not a history of drug abuse is obtained. Policemen should be alerted to the unique dangers of dealing with those individuals who have violent paranoid reactions to the drug. And. finally, schizophrenic patients who have any leanings towards drug experimentation should be warned that they are unusually sensitive to the adverse effects of PCP.

Further research is needed to determine whether there are more effective treatment methods for the PCP psychosis than what has been presented here. Research is also needed to document further PCP's adverse effects, and the Drug Enforcement Administration might consider whether this drug warrants reclassification under Schedule I.

PCP use is spreading rapidly because of ignorance of its unpredictable adverse effects among potential users, and because of the ease with which the drug is illicitly manufactured. It is important to increase awareness of PCP and its effects, as we might well anticipate a nationwide epidemic, an epidemic which, as far as we know, may exist even now.

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Chapter 15

Long Term Treatment of Adolescent PCP Abusers

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INTRODUCTION

The population described in this publication are residents in a licensed, social rehabilitation facility, known as Pride House. This 70 bed facility specializes in the treatment of adolescents with mental health and substance abuse problems. Males and females between the ages of 14 and 22 years are accepted into the program The mean age for the past two years has consistently approximated 16.5 years.

Over the years Pride House has developed a reputation for offering services to "difficult to treat" adolescents. Basic problems presented by these adolescents are as follows:

- Psychiatric illness such as depression, anxiety, character disorders, suicidal ideation, and schizophrenia.

- Substance abuse: approximately 95 percent of the client population are polydrug abusers who have ingested many substances ranging from marihuana to PCP and heroin. Some of these drugs have been ingested on a regular basis.

- Criminal offenses including grand theft auto, possession and dealing of drugs, pimping, prostituition, burglary, assault, running away, et cetera.

Most clients are referred to Pride House through the Probation and Social Welfare offices of Los Angeles County by a placement order from the courts. Clients are also referred from the majority of surrounding counties. In addition, there are a number of private referrals from hospitals, practicing psychiatrists, and psychologists in the area, as well as from local families. Most of these clients have had social-psychological profiles done by the referring institution's psychologist or psychiatrist. These profiles reveal that the majority come from broken homes. Approximately 78 percent of the total population come from single parent families: 45 percent come from divorced families; in the other 33 percent a parent was lost through death. The remaining 22 percent of the clients come from intact families.

Approximately 29 percent of the total population have been involved in aberrant family sexual behavior, primarily in the form of incest. This incestuous behavior is far more prevalent among the females than the males. Approximately 60 percent of females who have entered the program during the last six months report involvement in incestuous relationships with either parents, grandparents, or other members of the immediate family. To date, we have validated 23 percent of these reported incidents. The process of validation is ongoing and will continue for some time. Verification is difficult for clients who have left the program.

The majority of adolescents served by this program have been physically or emotionally battered and would qualify as "battered" children. Most are emotionally and educationally handicapped and have little opportunity to experience normal maturation and growth.

TREATMENT: GENERAL PROGRAM SUMMARY

Treatment of drug abusers in the context of an adolescent rehabilitation center has been specifically defined at Pride House. An initial prospect interview is done with each client. After this pre-intake interview is canpleted, the client's suitability for the program is evaluated. If the client is deemed suitable for Pride House, a lengthy diagnostic intake process is initiated. During the initial interview, a detailed personal, psychiatric, drug, family and social history is taken. An initial treatment plan is then formulated from these intake profiles. The treatment plan discusses existing relationships between the presenting symptoms and underlying psychopathology, and choice of drugs and the extent of drug use. This is especially important when the staff feels the client has chosen drugs as the major palliative of internal and/or external emotional conflicts. A basic assumption is that most adolescents coming to us are troubled and have chosen the use of drugs as the major vehicle to resolve these conflicts.

Substance abuse is seldom discussed during the course of therapy. In fact, the discussion of drug abuse during the therapeutic process is generally proscribed as antitherapeutic and distracting. This parallels our approach in working with all special problem areas. For instance, with homosexual clients the discussion of sexual activity is usually proscribed except in specific therapy sessions dealing with the sexuality of the client (Wellisch, De Angelis, and Paternite 1978). Our research has shown that youngsters will usually use their major behavior problem as the discussion focus in order to prevent the therapist from dealing with the underlying issues causal to their abnormal behavior.

Long term treatment includes a regimen of individual and group therapy, as well as family therapy. There is an educational program at Pride House which includes remedial mathematics, reading, tutoring and study for the California Proficiency and GED examinations. Pride House provides a complete and intense recreational program for the male population. Currently, the recreation program for females is not as sophisticated. The average number of hours of therapy per client each month is 36. Furthermore, 6.5 recreational sessions per resident per month are provided. In addition, 40-60 hours of teaching and tutoring activities per resident per month are available, excluding study time. On the whole, the milieu is totally supportive with little, if any, classical confrontation used. Generally, therapeutic approaches include Gestalt, Transactional Analysis, psychotherapy, and other supportive, humanistic, therapeutic regimes.

METHODOLGY

Initial investigation into the use of PCP in clients who entered Pride House during the last 6 months (from September 1977 through February 1978) identified approximately 50 percent of the population as either chronic or occasional PCP users. Chronic users were defined as those using at least 3-4 times a week and occasional users were identified as those using PCP once a week or less. This definition may seem arbitrary considering the powerful effects of PCP. However, our definition is similar to chronic PCP use as described by Fauman and Fauman (1978) who report use ranging from 2.5-5.8 days per week. This paper will report the results of our work with these PCP users/abusers.

Prospect and intake evaluation forms for 87 clients were analyzed in order to identify all PCP users in a 6-month cohort. Forty-five (45) clients representing 52 percent of the study cohort were identified as users of PCP. Clinical records of these 45 individuals were further analyzed to ascertain behavioral, familial, sexual, psychological, and other characteristics. The data collection form used is shown as appendix I.

After the data were collected, the information was sent to the Health Care Delivery Service Evaluation Research Unit. There, the data were validated and tallied, tabulated and analyzed as percentage differences. Results are provided in tables 1 through 7 and are discussed below.

RESULTS

Table 1 compares the demographic variables for (1) the occasional PCP user, (2) the chronic PCP user, and (3) the general Pride House population. In terms of sex, approximately fifty-eight percent (58.4 percent) of the general population are males as compared to 78.3 percent and 31.8 percent of the occasional and chronic PCP users, respectively. Females represent the majority of chronic PCP abusers (68.2 percent) while they are a minority of the general population (41.6 percent).

	OCCASIONAL PCP USER (n=23)	CHRONIC PCP USER (n=22)	GENERAL POPULATION (n=173)
	%	%	%
<u>SEX</u>			
MALE	78.3	31.8	58.4
FEMALE	21.7	68.2	41.6
TOTAL	100.0	100.0	100.0
<u>RACE</u>			
CAUCASIAN	87.0	81.8	64.7
BLACK	4.3	4.5	11.1
HISPANIC	8.7	13.6	21.8
OTHER	0	0	2.4
<u>AGE</u>			
MEAN	16.1 (yrs.)	16.3 (yrs.)	16.2 (yrs.)
RANGE	14 - 18	14 - 19	13 - 20

Only slight racial differences are seen a percentages of Caucasian, black and Hispanic chronic and occasional PCP users. However, there are greater percentages of Caucasians in the two groups of PCP users thah in the general Pride House population. Eighty-seven percent of the occasional users and 81.8 percent of the chronic users are Caucasians, as compared to 64.7 percent of the general population who were Caucasians.

Racial differences for degree of PCP use proved to be statistically insignificant ($X^2 = 0.28$; d.f. = 2; $.90 < p < .80$). However, the observed sex difference in PCP use proved to be statistically significant ($X^2 = 9.82$: d.f. = 1; $p < .01$). Females represented a greater proportion than males of the chronic PCP users. Mean age is approximately the same for the two PCP users groups and the general population. Only slight variations are observed in the age ranges for the three groups.

Table 2 describes frequency of PCP use for the sample. The largest proportion of occasional users ingested PCP once per week. Usage ranging from twice to several times month accounted for 34.8 percent of the occasional users. Approximately nine percent of the occasional users ingested PCP only once per month.

The majority of chronic users (61.9 percent) ingested PCP on a daily basis. About thirty-eight percent used PCP three to four times per week.

Equally significant is the extremely high daily use of drugs other than PCP in both groups. Approximately 86 percent and 91 percent of both the occasional and chronic use groups, respectively, ingested a variety of drugs on a daily basis. Therefore, it is safe to assume that both groups are chronic drug abusers, with one group supplementing its other daily drug usewithheavy PCP usage.

While occasional and chronic users show about the same percentages displaying depressive symptomatologies (table 3), they differ quite drastically in other clinically observed behaviors. Comparisons in terms of anxiety show that 44.8 percent of the occasional users exhibited anxiety symptoms as compared to only 7.7 percent of the chronic users. On the other hand, 30.7 percent of the chronic users were described as having character disorders as compared to 3.4 percent of the occasional users. Interestingly, while clinical management of chronic PCP users is similar to that of schizophrenic adolescents, neither the occasional nor the chronic users were diagnosed as being schizophrenic. Accurate diagnosis of this illness is even more difficult in a drug abusing population. In the past, Pride House has treated adolescents who have been diagnosed as schizophrenic. None of the present cohort displayed symptoms or behaviors which would result in such a diagnosis.

In other work with this population, we have uncovered relatively large numbers of cases wherein clients have been sexually molested or violated (incest). Approximately 32 percent of chronic PCP users report sexual molestation and/or incest. In the occasional

FREQUENCY OF USE

FREQUENCY OF USE	OCCASIONAL PCP USER (n=23)		CHRONIC PCP AND OTHER DRUGS USER (n=22)	
	PCP	OTHER DRUGS	PCP	OTHER DRUGS
	%	%	%	%
DAILY	0	85.7	61.9	90.9
3-4 TIMES A WEEK	0	14.3	38.1	9.1
ONCE A WEEK	43.5	0	0	0
TWICE A MONTH	13.0	0	0	0
THREE TIMES A MONTH	17.4	0	0	0
SEVERAL TIMES A MONTH	17.4	0	0	0
ONCE A MONTH	8.7	0	0	0
TOTAL	100.0	100.0	100.0	100.0

TABLE 3

PSYCHIATRIC DIAGNOSES

TYPE OF PSYCHIATRIC DIAGNOSIS (MULTIPLE RESPONSE)	OCCASIONAL PCP USER[(a)] (n=23)	CHRONIC PCP AND OTHER DRUGS USER[(b)] (n=22)
	%	%
DEPRESSION	51.7	61.6
ANXIETY	44.8	7.7
CHARACTER DISORDERS	3.4	30.7
TOTAL	100.0	100.0

(a) 29 responses obtained

(b) 26 responses obtained

PCP use group this was universally absent. Chi square (x^2) was calculated and the differences between the two groups were found to be significant ($X^2 = 8.67$; d.f. = 1; $p < .01$).

We investigated the behavior of PCP abusers within the treatment milieu. This was important in light of the common belief that PCP abusers are hostile and disruptive. Table 4 verifies this belief to some extent. Surprisingly, the occasional users of PCP acted out in an angry or belligerent manner far more often than the chronic users. Sexual acting out was much more prevalent for the chronic PCP user (30.8 percent) than for the occasional PCP users (12 percent). Hostility was displayed at about the same level in both groups, but the chronic users reported themselves as delusional, while occasional users did not ($X^2 = 7.46$; d.f. = 3; $< .10$ $p < .05$).

Table 5 shows that chronic PCP users were more likely to commit rule infractions based on sexual conduct(49.9 percent) than occasional PCP users (39.0 percent). On the other hand, occasional PCP users were more likely to commit drug-taking infractions (73.7 percent) or violent acts (12.9 percent) than chronic users. Chronic users violated drug rules 68.2 percent of the time and commited acts of violence only 4.5 percent of the time. It should be noted that violent behavior is defined as extreme verbal abuse as well as such activities as destruction of property and vandalism. No violent acts against persons have been recorded in either group.

For both occasional and chronic users, drug-taking is the most frequently occuring rule infraction. Acts of violence are the least frequently occurring infraction.

Table 6 verifies the data presented in the previous table. When all rule infractions are totalled it can be seen that drug-taking predominates in both the occasional and chronic use groups. Sexual misbehavior is the second most frequent rule infraction, and violent behavior is the least frequent.

We also investigated length of stay or program retention rate of chronic, occasional and non PCP-using residents. Table 7 demonstrates that chronic PCP abusers remain in the program longer,on the average, than the other groups. No statistically significant difference was found when length of stay for occasional users was compared to chronic users. On the other hand, statistical significance was achieved when length of stay of all PCP users was compared to an equal nunber of non PCP users ($t = 2.29$; d.f. - 74; $p < .05$). T-tests were computed after excluding members of both comparison groups whose length of stay was far beyond the standard deviations ($n = 39$ PCP users; $n = 37$ non PCP users). Nevertheless, it should be noted when all data for length of stay were included in the computations, the computed t-value was 1.98.

DISCUSSION

It is difficult to compare our results with published reports of

262

TABLE 4

TYPE OF BEHAVIOR DISPLAYED

TYPE OF BEHAVIOR (MULTIPLE RESPONSE)	OCCASIONAL PCP USER (n=23)	CHRONIC PCP AND OTHER DRUGS USER (n=22)
	%	%
ANGRY/BELLIGERENT	80.0	46.2
ACTING OUT/SEXUAL	12.0	30.8
HOSTILE	8.0	11.5
DELUSIONAL	0.0	11.5
TOTAL	100.0	100.0

TABLE 5

FREQUENCY OF ABERRANT BEHAVIORS

FREQUENCY OF SEX, DRUG, VIOLENT BEHAVIOR	OCCASIONAL PCP USER (n=23)			CHRONIC PCP AND OTHER DRUGS USER (n=22)		
	SEX %	DRUG %	VIOLENT %	SEX %	DRUG %	VIOLENT %
NONE	60.9	26.2	87.0	50.0	31.8	95.5
ONCE	13.0	30.4	4.3	27.2	18.2	4.5
TWICE	17.4	30.4	4.3	18.2	31.8	
THREE	4.3	4.3		4.5	9.1	
FOUR						
FIVE						
SIX	4.3					
MORE THAN SIX		4.3			4.5	
TOTAL	100.0	100.0	100.0	100.0	100.0	100.0

TABLE 6

OCCURRENCE OF PROGRAM RULE INFRACTIONS

OCCURRENCE OF PROGRAM RULE INFRACTIONS (MULTIPLE RESPONSE)	OCCASIONAL PCP USER[a] (n=23)	CHRONIC PCP AND OTHER DRUGS USER[b] (n=22)
	%	%
SEXUAL	27.6	37.0
DRUG TAKING	62.1	59.3
VIOLENT	10.3	3.7
TOTAL	100.0	100.0

[a] 29 responses obtained
[b] 27 responses obtained

TABLE 7

LENGTH OF STAY COMPARISON

CATEGORY	MEAN LENGTH OF STAY	t-TEST; OCCASIONAL	t-TEST; ALL PCP VS. NON PCP USERS[a]
NON PCP	$\bar{X}$ = 67.76 S.D. 56.71 n = 42		
OCCASIONAL PCP USER	$\bar{X}$ = 85.32 S.D. 73.62 n = 22	t=0.99 d.f.= 42 $0.50 < p < .10$	t=2.29 d.f.= 74 $.05 < p < .02$
CHRONIC PCP USER	$\bar{X}$ = 108.18 S.D. 79.18 n = 22		

[a] t-tests between all PCP vs. non PCP users done initially included extremes of stay. Corrected t-tests were performed eliminating 3 lower end 2,3,3,6,13,13 and 2 upper end 225,226,276,316 lengths of stay for each group. Both ends far exceeded standard deviations and high end represents lengths of stay longer than present study period. When all of these days are included the t-test was as follows: t=98; d.f.=84; $0.10<p<0.05$; a t of 1.99 would have been significant at the 0.05 level.

PCP use. Most of the previous studies used "ever used" and "never used" categories, whereas we chose "occasional" and "chronic" use categories. Lerner and Burns (1978) and Fauman and Fauman (1978) reported that males constituted the majority of their samples (68.7 percent and 80.0 percent respectively). In our study this is true only of the occasional user. Chronic use was much more prevalent for females.

In terms of race, the Faumans report the highest use for blacks. Lerner found that Caucasians predominated in his work. Our findings parallel Lerner's, since Caucasians predominate in our population. This my be due to our treatment program's physical location in a suburb of Los Angeles that is predominantly Caucasian. Most referrals to our program over the last four years have been Caucasian youth. No significant age differences exist between the population we have studied and those studied by Lerner and Burns and the Faumans.

Approximately fifty-two percent (51.7 percent) of our entire sample cohort (87) reported use of PCP. The Faumans report 66.6 percent of the treatment population which they studied used PCP, while Lerner and Burns report 31.8 percent use in their study. Our similarity to the Faumans' results may be due to similar residential treatment program milieus, whereas Lerner and Burns'data are taken from DAWN and the National Youth Polydrug study.

Approximately forty-nine percent (48.8 percent) of out study cohort who used PCP were classified as chronic users. Lerner and Burns (1978) reported 35.6 percent of PCP users in their study had used PCP with the same frequency.

Both the chronic and occasional users reported high usage of drugs other than PCP. This is not surprising when the following are considered: (1) These clients are in a social rehabilitation program known to treat all types of drug abuse, and (2) polydrug combination with the increased psychopathology observed in the polydrug abuser (Bienvenuto and Bourne 1975; Raynes, Patch, and Cohen 1975) my help to explain the high percentage of reported anxiety, depression and character disorders found in our study population. These clients may be ingesting drugs in an effort to reduce the psychic and emtional distress which they are experiencing.

Of foremost importance is that we have diagnosed little or no schizophrenia in this population. Perhaps this is due to our unwillingness to label a child as schizophrenic simply because his or her behavior does hot fit the norm. This may account for the little difficulty we have had in working with PCP-abusing youth.

A significantly larger proportion of chronic PCP abusers in our sample report sexual molestation and/or incest. We have had no explanation for this other than to offer the possibility that. PCP provides a drug-induced respite from the emotional pain and anger suffered by most of our adolescent clients who have had these experiences. Perhaps PCP intoxication controls this rage at some stage of the intoxication. It may be that as the drug effects diminish, the suppressed anger may surface in the form of overt hostility, belligerence and verbal abuse which we witness. The long term acting out observed with clients in residential treatment settings may represent an extended and necessary catharsis which offers an excellent opportunity for therapeutic intervention.

Although differences were seen in the types of behavior displayed by PCP users, statistical differences were not achieved when the groups were compared. Both groups act out; the type of acting out may be influenced by drug states or therapeutic milieu. We have no way to determine this at the present time.

The fact that chronic PCP abusers stay in treatment longer than non PCP or occasional PCP users, is probably the most important practical finding of this study. If one assumes that chronic users are more in need of treatment than other types of drug users,then length of stay is an important therapeutic variable, since therapeutic intervention takes time to have effect. Whether or not chronic abusers stay longer because they are more troubled and realize they need help, or whether our therapeutic interventions are effective with this group is difficult to detemine. Perhaps it is safe to say that were our therapeutic endeavors not effective, the more troubled PCP abusers would leave. The increased length of stay may indicate that whatever conflict resolutions were provided by PCP use are provided by the treatment staff. This will be discussed in more detail below.

TREATMENT CONSIDERATIONS

Occasional users of PCP having no history of long term effects are treated similarly to all other clients in the program admitted for substance abuse treatment. In effect, staff and client expectations are the same for the occasional PCP abuser as for the general population. With the exepction noted below, all clients participate in all normal therapeutic activities, taking responsibility in the program, attend school, et cetera. Therapeutic responses are dictated by the client's present behavior, combined with our knowledge and understanding of the child's family and personal history. The client's abuse of PCP at one point in his/her life is considered fairly irrelevant within the context of the milieu.

As shown in tables 1, 3, 4, 5, and 6, clinical differences exist in psychiatric diagnoses, acting out behaviors and program rule infractions. These differences do not necessarily mean that clinical interventions in the PCP-using group need be dramatically different than those in non PCP-using groups of adolescents which we treat. Anxiety and depression, commonly seen in our general population, are treated similarly to the same states seen in PCP abusers. Program clinicians target their efforts at the behavior and symptoms rather than on a substance(PCP)which may or may not be the cause of these reactions. As shown in table 4, occasional users are often angry and/or belligerent. Clinically this is handled as is any angry confrontation with a client. However, in the PCP population staff is more aware of the frequency of an angry reaction and is prepared for this response. It is important that staff anticipate these angry outbursts in order to take control and demonstrate an understanding of the situation.

Both the occasional and chronic PCP users have little difficulty integrating into the general population and responding to treatment. As mentioned, PCP users stay in treatment longer than non-users. (Certain clinical differences are observed between chronic PCP users, occasional users, and the general population. The treatment of chronic PCP abusers coming into Pride House with histories of adverse drug reactions is somewhat different from the treatment of the general population. In many ways, treament simulates our work with schizophrenic and other very troubled youngsters.

Basically, PCP abusers who enter the program and are past the acute intoxication phase are treated as follows:

- Minimal confrontation or hostility-provoking behavior cm the part of staff or other clients is the rule.

- Particular care is taken to provide PCP users a non-threatening environment in which they can begin to feel comfortable.

- Minimal involvemnt in specific therapeutic intervention is expected immediately.

Many PCP users display flattened affect, depression, agitation, hostility and belligerence. They are usually unable to cope with the demands and expectations of a structured, intensive therapy regimen. With these clients, staff expectations are drastically lower. This means that the PCP abuser is not expected to participate extensively in either group or individual therapy, school or recreation programs. It is understood that he/she may be belligerent and refractory to treatment. Hostility, agitation, and depression, as well as memory loss and motor impairment are considered part of the pathology to be treated, rather than major impeding problem. A program of support and reinforcement is provided both within the milieu and in therapy.

Drug therapy, either with the administration of tricyclic antidepressants or tricyclic and other antipsychotic agents is minimal. Use of these agents has not been shown to be effective and caution has been urged in their application in treating PCP abusing clients (Varippa 1977).

Certain acting out behavior is tolerated in these clients, more so than in clients having no history of PCP abuse. Generally, acting out behavior takes the form of extreme verbal abuse. We assume that these outbursts of anger and hostility will occur and we work with them, rather than prohibit the behavior and thereby exacerbate the situation.

Finally, another aspect of dealing with PCP abusers is a remedial education and tutoring program. It is therapeutic to help a young client understand that any existing memory loss and/or motor impairment is most likely a drug related event and will usually reverse itself over a period of time. At this point, careful tutoring and handling by the education staff are very important. In this way, the client is actually engaged in a therapeutic process (school), yet not expected to do "therapy." Individual attention provided by the educational tutors, coupled with the educational testing and the learning diagnostician's work, give the client a sense that he/she will soon be able to function normally.

ACKNOWLEDGMENTS

The authors would like to thank V.Tokita and D.Marple for their technical assistance.

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APPENDIX I

USE PATTERNS

CATEGORY	NON PCP USER	OCCASIONAL PCP USER	CHRONIC PCP ONLY USER	CHRONIC PCP & OTHER DRUGS USER	NON DRUG ABUSER
1) Family Marital Status					
Married					
Separated					
Divorced					
Single by death					
2) Sexual Molestation/Incest					
3) Psychiatric Diagnosis					
Depression					
Anxiety					
Schizophrenia					
Character Disorders					
4) Behavior					
Angry/Belligerent					
Acting out/sexual					
Hostile					
Delusional					

(Continued)

APPENDIX I (continued)

CATEGORY	NON PCP USER	OCCASIONAL PCP USER	CHRONIC PCP ONLY USER	CHRONIC PCP & OTHER DRUGS USER	NON DRUG ABUSER
5) Drug Use Upon Program Entry					
Multiple with PCP					
Multiple no PCP					
PCP only					
Frequency of use (PCP)					
Frequency of use (other drugs)					
6) Demographic Characteristics					
Sex: Male/Female					
Age: Mean/Range					
Race: Caucasian					
Black					
Hispanic					
Other					
7) Program Rule Infractions					
Sexual behavior					
Drug taking behavior					
Violent behavior					
Frequency (sex)					
Frequency (drugs)					
Frequency (violence)					

Chapter 16

Phencyclidine, Criminal Behavior, and the Defense of Diminished Capacity

Ronald K. Siegel, Ph.D.

"The cause of the world-wide consumption of hashish, opium, wine, and tobacco," wrote Leo Tolstoy (1890), "lies not in the taste, nor in any pleasure, recreation, or mirth they afford, but simply in man's need to hide from himself the demands of conscience." Tolstoy argued that men "stupefy" themselves with drugs that make them commit actions contrary to conscience. He cited robbery, rape, and murder as examples.

Modern courtrooms in the United States are becoming increasingly plagued by examples of such drug related acts, acts which would have surely outraged Tolstoy's 19th Century moralism and supported his notion that man is an "animal being." The magical elixir which is usually credited with this transformation of man from a "spiritual being" to an "animal being" is phencyclidine (PCP). Perhaps more than any other drug, with the exception of alcohol, PCP is becoming increasingly conspicuous in both criminal behavior and in the criminal defense of diminished capacity. Diminished capacity itself is a "defense in which criminal culpability is gauged upon various mental states. If the defense is proven, it can reduce the degree of the crime or even result in an acquittal" (Schwab 1976).

A young man smokes some PCP and proceeds to rob a gas station at gunpoint. A juvenile smokes PCP and rapes his baby sister. A witness to a fatal stabbing is admittedly intoxicated with PCP but claims to remember clearly all the events. A witness to another murder claims to be intoxicated with PCP and amnesic for most of that time. A police officer encounters a young man who may have ingested an analog of PCP. The man, naked and unarmed, reportedly becomes combative and assaultive and is shot to death by the officer. Two lovers are smoking PCP alone in their bedroom. Within a few minutes one is bleeding to death from a knife wound which may or may not have been self-inflicted. A middle-aged woman takes some cocaine which has been adulterated with PCP and tries to rob a bank armed only with a broom which she manipulates as if it were a gun. In these and many similar cases the law enforcement and judicial systems are turning more and more to expert witnesses in order to help clarify the effects of PCP on behavior. The process is rapidly defining a new field: forensic psychopharmacology. Forensic psychopharmacology can be considered the application of the study of drugs and behavior to legal issues. The present chapter attempts to discuss aspects of PCP-induced behavior which can be applied to legal issues.

DRUGS AS SCAPEGOATS AND THE ORIGINS OF DIMINISHED CAPACITY

Psychopharmacology is essentially the study of drugs and behavior. The underlying lay assumption is that drugs inevitably affect behavior. A corollary is that abnormalities in behavior often may be blamed on drugs. In his critique of the drug abuse field, psychiatrist Thomas Szasz (1974) noted that this assumption has led to the persecution (and prosecution) of drugs, drug users, and drug dealers throughout history. Indeed, even in their linguistic roots drugs have been associated with scapegoats. The *pharmakos* in ancient Greece was the human who was sacrificed as a scapegoat in primitive ceremonies. Later, when human sacrifice was abandoned in Greece, the term *pharmakoi* came to mean "human medicine" and was applied to poisons and drugs. The classic association of drug-induced altered states of consciousness and diminished capacity was most dramatically portrayed throughout the tragedies of fifth century Greek playwrights. The association of drugs with scapegoats has been with us ever since those times.

In Euripides' The Bacchae, Agave, the bacchante queen, kills her son, Pentheus, in an altered state which was probably a combination of alcohol intoxication and religious hysteria (Emboden 1977). Agave believes she has killed a lion as a scapegoat, and the murder itself is perhaps one of the most gruesome in the annals of psychopharmacology, rivaling even the Tate-LaBianca murders of the present century:

> But she was foaming at the mouth, and her crazed eyes
> rolling with frenzy. She was mad, stark mad,
> possessed by Bacchus. Ignoring his cries of pity,
> she seized his left arm at the wrist; then, planting
> her foot upon his chest, she pulled, wrenching away
> the arm at the shoulder--not by her own strength,
> for the god had put inhuman power in her hands.
> Ino, meanwhile, on the other side, was scratching off
> his flesh. Then Autonoë and the whole horde
> of Bacchae swarmed upon him. Shouts everywhere,
> he screamed with what little breath was left,
> they shrieking in triumph. One tore off an arm,
> another a foot still warm in its shoe. His ribs
> were clawed clean of flesh and every hand
> was smeared with blood as they played ball with scraps
> of Pentheus' body (Euripides, p.204).

Emerging from that intoxicated state, Agave realizes that what she has killed is not a lion but her son. Agave confused the reality in which she confronted a lion with the reality in which she confronted her son. Crucial to an understanding of the lay are the Greek concepts of *sophia* (meaning wisdom, skill , expertise) and *amathia* (meaning uncontrolled violence). Specifically, *sophia* implies a firm awareness of one's own actions, judgements, and morals. Conversely, *amathia* means an uncontrollable ignorance of one's actions and capacities, someone prone to violence, harshness, and brutality. In its essence, Euripides' play tries the case on the merits of diminished capacity *(amathia)* versus premeditation and intent *(sophia).* A modern day defense attorney might argue that Agave was diminished in capacity as a result of both the alcohol and religious intoxication. A prosecutor might successfully argue (and win a first degree murder conviction) that the killing was motivated, since Pentheus bitterly opposed Agave's involvement in Dionysian rites and Agave knew it all along. However, the jury at the time--the Greek chorus in the play--finds Pentheus guilty of *amathia* because he want only and violently refused to accept the necessity of the Dionysian rites (wine, dance, and religious ecstasy), thus committing an immoral act against a god Accordingly, Agave is declared *sophia* in supporting the sacrificial rites. While the judge, Dionysus himself (who could be challenged in a modern courtroom for obvious prejudice), finds the murder justified, he banishes Agave from the city forever. The verdict of the play is probably the equivalent of voluntary manslaughter with absence of malice due to diminished capacity. Thus concluded history's first diminished capacity trial.

INTOXICATION AND BEHAVIOR

The case discussed above is important in emphasizing the numerous variables that can influence drug-induced intoxication and behavior. Although the definition of the word intoxication (which comes from the Latin *intoxicatio,* meaning poisoning or inebriation) is far from precise, one that is generally accepted in pharmacology and medicine is "the abnormal state induced by a chemical agent....excitement or exhilaration beyond self-control." Pollack (1976) defines such intoxication for legal purposes as:

> a temporary state of mental impairment due to drugs or alcohol in which the alcohol or drug influence creates a mental impairment that makes the person unable to form the specific intent for the crime charged against him, although the defendant committed an illegal act at the time.... Intoxication is thus a clinical condition that is defined by clinical signs and symptoms, ranging from mild, moderate, to severe, with coma and eventual death (p. 258).

This clinical condition can be modified by a wide variety of variables, including both drug variables and user variables. Among the important drug variables are: preparation and purity, dose, route of administration, rate of ingestion of the drug, rate of absorption, site of action, rate of metabolism, rate of elimination, mechanism of action? and others. Among the important user variables are: individual variability, age, sex, weight, general state of health, medical history, drug history, behavioral history, presence of other psychoactive agents (prescription and nonprescription drugs), personality, psychological set (attitudes, expectations, etc.), setting (physical environment and psychological state of others present), and others. The more specific this information is, the more precise can be the description of drug induced behaviors and the stronger can be the opinion of the expert witness in court. While a full understanding of these interactions is presently restricted by limited knowledge about phencyclidine, the presence of such a myriad of variables should temper a desire to simplify behavior with labels such as *sophia, amathia,* "diminished capacity," "criminal responsibility," "legal insanity," "mental incompetency ," "unconscious ," "psychotic ," "loaded," "dusted," "toasted," "stoned," "wasted," or even "high."

PHENCYCLIDINE AND BEHAVIOR

The nature of phencyclidine-induced effects on behavior are discussed in several sections elsewhere in this volume. The nature and phenomenology of phencyclidine intoxication are also described more fully in another chapter (see "Phencyclidine and Ketamine Intoxication: A Study of Pour Populations of Recreational Users," by Siegel, this volume). Only those behaviors which are characteristic of intoxication for purposes of diminished capacity defenses or for purposes of understanding criminal behavior are discussed here.

While phencyclidine remains medically classified as an anesthetic agent, it is well known that intoxication with the drug can be marked by excitatory, sedative, hallucinatory, catatonic, and even seizure behaviors. These apparently paradoxical reactions have prompted numerous investigators to re-examine the effects of phencyclidine on the brain and behavior. In an important series of preclinical studies with animals, Winters and his coworkers (e.g., Winters et al. 1967) have demonstrated that there is a progression of effects following increasing doses and these differ considerably from the modes of action of most anesthetics but compare more closely with most hallucinogens. like LSD. This progression forms a continuum ranging from an awake state, to a hyperactive aroused state, to a state of inappropriate movements, to a state of unresponsive behavior, to generalized seizures, and to death. In animal studies with cats these states are marked by changes in both behavior and electroencephalograms (EEGs). The progression is described in the following way:

> The initial effects of administration of phencyclidine consisted of cortical desynchronization and development of hippocampal theta waves. After 5 to 6 minutes, intermittent and then continuous hypersynchronous bursts appeared accompanied by inappropriate movements of the head. Within 15 minutes an increase of amplitude and a decrease of frequency of the hypersynchrony, separated by short periods of desynchronization, were observed. At this time the animal (cat) was crouched, unresponsive to stimulations, had a fixed gaze, pupillary dilation, salivation and increased muscle tone. Desynchronization became more prominent and finally a generalized high frequency high voltage seizure pattern appeared which was accompanied initially by limb twitching, then generalized convulsions (Winters et al., 1967, p. 75) .

In man, there are four basic types of behavioral responses to these excitatory states of the central nervous system. Initially the user becomes excited in terms of motor activity and this is usually accompanied by mood elevation. Secondly, as excitation increases, the mood becomes euphoric but the motor behavior becomes ataxic. Thirdly, further excitation produces bizarre and inappropriate motor movements coupled with subjective reports of hallucinatory intoxication. Fourthly, a state of epileptoid activity is reached which is marked by myocionic jerks and generalized seizures. At this point the user may appear cataleptic and subsequently report amnesia for the experiences.

Typically, when PCP is smoked, the onset of symptoms appear within 2 to 5 minutes (Burns and Lerner 1976). These authors also report that a peak, plateau, or “high” period ensues for 15 to 30 minutes followed by a “loaded” period of 4 to 6 hours. Recovery time to normal behavior may take from 24 to 72 hours or longer. Indeed, some cases may require as long as 15 days for behavior to become alert, oriented and normal. During such intoxications, PCP can be detected in blood or urine but detected levels are not necessarily associated with specific behavioral states (Reynolds 1976). Burns and Lerner (1976) and Siegel (this volume) offer numerous clinical features of both the acute confusional state or delirium (low to moderate doses) and the state of stupor or coma (high doses). Some of these features are discussed in the sections which follow.

CLINICAL ENCOUNTERS WITH INTOXICATED INDIVIDUALS

Typically, the vital signs of the PCP-intoxicated person would indicate normal or slightly increased respiratory rate, increased blood pressure, increased pulse, and normal or slightly increased temperature. In terms of the motor system, the gait may be grossly ataxic and the person may be unable to stand or walk properly, perhaps due to increased muscle tone and rigidity. The body movements may appear restless, repetitive, and often facial grimacing is observed. High doses can produce "purpose-less movements," muscle tremors and twitching, and generalized motor seizures which are unpredictable in frequency or duration. Other features include: repeated episodes of vomiting (produced by the central action of the drug); increased salivation, tearing, and perspiration; and increased discharge of mucus from the nose, mouth, and throat.

With low doses or during early stages of high dose intoxication, the person would initially appear responsive, awake, and capable of responding to simple yes/no questions. Speech, however, is commonly slurred (dysarthria). As intoxication progresses through the continuum of excitation, verbal responses to yes/no questions may be replaced by simple nodding or facial gestures. This usually results from increased slurring which progresses to stuttering and extreme difficulty in speaking properly. The user may simply "give up" trying to verbalize, but this does not necessarily imply attentional dysfunction. Indeed, sensation is heightened at this point, and the user may have increased sensitivity to visual and auditory stimuli. Conversely, some individuals may appear more talkative and communicative, but this is rare. Individuals are usually disoriented in both time and space and consequently may appear confused and even fearful, especially if environmental stimuli are overly intrusive or intense.

However, in deprived environments, such as dark and quiet rooms, these clinical features may be absent. Since the brain is in a state of hyperexcitability, it is not surprising to find that the user will be unable to sleep or rest during acute intoxication. The eyes remain open in low dose conditions ("stare" appearance) and sometimes the upper eyelids droop due to the sympathetic innervation induced by PCP. High doses may cause the eyes to close but the user is still clinically awake, although s/he may not respond to stimuli. Examination of the eyes may reveal additional findings. Low doses have been characterized by an inability to fixate, and the eyes may appear to gaze independently at different points. Attempts to control and fixate the vision may result in involuntary, abrupt, and rapid movements or jerks of both eyes. High doses simply exaggerate these symptoms which have been described as "roving eye movements" and "doll's eye movements." In both high and low dose intoxications, intermittent horizontal and vertical nystagmus as well as a decreased or absent corneal reflex have been noted.

POLICE ENCOUNTERS WITH INTOXICATED INDIVIDUALS

When encountering PCP-intoxicated individuals, law enforcement officials frequently observe some of these characteristic clinical features. Specifically, speech is usually described as slurred, the gait is unsteady, and the eyes glassy, staring, or blank. Consider the followed edited excerpts from the reports of arresting officers:

> Subject's speech was slurred and at times subject was unable to talk. Subject's reactions were very slow. In officer's opinion the subject was under the influence of a drug.
>
> He was oblivious to all of the occurrences around him, and walked about in a dazed condition. It was the arresting officer's opinion that the minor was under the influence of a hallucinogenic drug, possibly that of PCP.
>
> Suspect looked in officer's direction and immediately tensed up. He stopped and his anns went stiff. As officer exited his vehicle and approached suspect, officer noted his breathing to be extremely heavy. The suspect's eyes bulged and he began to lick his lips as he looked about numerous directions.

Of course, such observations alone, while helpful to the forensic psychopharmacologist, may not indicate intoxication per se. Indeed, arresting officers are frequently misinformed as to the nature of drug-behavior interactions, and there is admittedly a paucity of police knowledge concerning PCP use itself (Overend 1977). One police officer told the author that "the smell of a minty breath" was characteristic of his encounters with PCP users. While PCP is frequently smoked on mint leaves, without observation of other clinical features of intoxication, smell alone is insufficient to warrant the presumption of PCP use. Other police officers are beginning to attribute any bizarre behavior, even some motor vehicle violations, to PCP intoxication. Reynolds (1976) reports that in nine such cases, seven suspects failed field sobriety tests, while the remaining two individuals were judged incapable of even attempting tests.

Police encounters with PCP-intoxicated individuals are frequently associated with violent, assaultive, combative, suicidal, and even homicidal behaviors, In most such cases, the intoxicated individual is hyperexcitable, hypersensitive, disoriented, and confused. Therefore, violent and aggressive reactions can be triggered in these individuals by common police practices including: interrogation, detainment, physical contact, restraining holds, handcuffing, and general arrest procedures. Even seemingly mild stimuli, such as shining a flashlight in a suspect's eyes, may trigger aggressive behavior. Aggression induced by PCP may take the form of fear, flight, or fight reactions. The nature of the reaction can be influenced by the police officer's own behavior and approach to the individual. Mild verbal behaviors and minimal physical contact are usually indicated (see "Clinical Management of the Phencyclidine Psychosis;' by Luisada and Brown 1976). Nonetheless, violent encounters occur frequently. Consider the following edited excerpt from an arresting officer's report:

> The suspect vehicle driver exited the vehicle and attempted to flee. He stopped abruptly and stared at the arresting officers who were approaching on foot. Suspect ignored the arresting officers' demands to lay on the ground. Arresting officers forced him to the ground and attempted to handcuff him. Suspect displayed a phenomenal strength and said absolutely nothing. Sgt. C. and Officer R. assisted the arresting officers in subduing the suspect, which took approximately 1 1/2 to 2 minutes. During that time, the suspect was struck several times on the right elbow and arm in attempt to force same behind him for handcuffing. Such striking had no effect at all on the suspect's resistance. Officer R. finally used a carotid choke hold to render the suspect unconscious.

Not all aggression is emitted by the intoxicated individuals. Unaccustomed to the often bizarre and inappropriate behavior of phencyclidine users, police officers occasionally react with considerable force. Arrest techniques for suspects involve an "escalation process" of control. Techniques range from "no contact" with a cooperating suspect to "deadly force" for use in situations of life-endangering attack. Under certain circumstances where the suspect becomes violent, unconsciousness-rendering holds are considered necessary. These holds include the "bar arm" hold (forearm across the front neck) and the "carotid hold" (pressure on carotid artery). Durning the process of escalating force, the police officer depends, to some extent, on the reactions of suspects to force or pain (threatened or actual) in order to gauge appropriate levels of force. The PCP intoxicated suspect is often analgesic, feels no pain, and thus deprives the officer of much of the deterrent value of his force. In addition, unconsciousness-rendering holds on PCP-intoxicated individuals may complicate the respiratory difficulties seen in cases of toxic overdose. Contact force with police batons or other weapons runs the risk of provoking hyperexcitability and even triggering psychomotor seizures. Probably the best procedures are those that employ manual restraint by several (3-4) officers. Officers and users alike would be well advised to note those final words in Leary, Metzner, and Alpert's (1964) guide to handling hallucinogenic emergencies: "Remain calm, remember the teachings" (p. 159) . Otherwise, the escalation process may run its full and tragic course. Consider the following account from the Los Angeles Times (Overend 1977):

> While the controversy continued over the fatal shooting of a 35-year-old biochemist by a Los Angeles policeman, the county coroner's office confirmed earlier this month what narcotics officers had suspected since the morning of Aug. 4. It was then that (the victim), described by friends and relatives as a "nonviolent and peaceful man," was shot to death while allegedly resisting arrest after being spotted at 5:30 a.m., naked and trying to climb a street sign near his Laboratory. The coroner's report that traces of a drug similar to PCP, also known as angel dust, had been found in (the victim's) blood did not resolve the issue of whether the policeman was justified in shooting (6 times at close range) the unarmed man. It remained for the legal system to determine that (p.2).

STATEMENTS OF INTOXICATED INDIVIDUALS

When the legal system tries to determine the role of PCP in cases such as the one discussed above, statements made by the intoxicated individuals, either to arresting officers or witnesses, can be as helpful as the clinical observations themselves. Even when intoxicated individuals make no statements, subsequent examination and interviewing by a skilled forensic psychopharmacologist may probe for and elicit information regarding the specific phenomenology of PCP intoxication (see Siegel, this volume) . However, owing to the possibility of confabulation, post-hoc statements must be accepted with extreme caution. While such statements are hearsay and cannot be admitted in court, they do add to the weight of the examining expert's opinion. Several types of statements seem characteristic of PCP intoxication, but by themselves are insufficient proof of such intoxication. The following edited statements are typical of those made to police or witnesses:

> I was smoking Dust. I had two hits. That was bad stuff. (Statement later denied by suspect).

> I was smoking Dust and got really whacked out. Like I was driving in a dream, felt funny at times. We were laughing a lot, riding the bumps and floating. I remember hitting another car, someone telling me to get out of the car, and waking up at the police station.

> I thought I had been shot by the police at the party and I started running and fell to the ground. Then I was attacked by black widow spiders. They were over everyone and all over me. It was like a dream.

> Everything was loud, real loud. Lights were very bright. It was a trip. I don't remember a lot. I got sick of it and threw up.
>
> She tried to jump out the window through the glass. I pulled her back once. She was Busted. She said she can fly.
>
> I couldn't walk. I don't know where I am. I don't remember anything.
>
> It was like tying myself in knots. I couldn't communicate. I got mad, screamed, cried. They were all afraid of me.
>
> I was feeling out of my body and liked it. It's all right.
>
> It could have been a dream. To be honest, I don't know if I was physically up there (indicating scene of crime) or spiritually there.
>
> I felt spaced, things were for real but distorted. Things were moving, patterns overlaying things and people, patterns projected onto people.
>
> My hands won't fit in there (indicating handcuffs). They're all swollen and big. Too big.
>
> You guys (indicating officers) seemed so far away. Miles away. I thought I had plenty of time. What a trip. Wow!

THOUGHTS OF INTOXICATED INDIVIDUALS

Even when overt verbal statements or other motor behaviors are absent, the PCP- intoxicated individual may engage in a wide variety of cognitive processes. An appreciation of these inner subjective thoughts and mental images will enable a better understanding of PCP-induced behaviors and possible criminal actions. Such knowledge also may help in both predicting and controlling behavior when encountering intoxicated individuals.

Two stages of intoxication can be distinguished: the acute stage and the psychotic stage. The acute stage results from recreational patterns of intoxication which are discussed elsewhere (Siegel, this volume). The psychotic stage may occur from acute usage, but it more often represents high dose or chronic administration, and the psychosis may not be manifested until several hours or even days later. Only data from acutely intoxicated individuals are discussed here and such individuals may differ substantially from those seen in the psychotic stage by other authors (e.g., Fauman et al. 1976; Luisada and Brown 1976) .

Traditionally, psychologists consider cognitive processes to include perception, learning, and thinking, since they all deal, to some extent, with the problem of knowledge (including the knowledge of right and wrong). Perception can be defined as the process by which an individual receives or extracts certain information about the environment, Learning is defined as the process by which this information is acquired through experience and becomes part of the individual's storage of facts (memory). Thus, the results of learning facilitate the further extraction of information, since the stored facts become models against which cues are judged. The most complex of these cognitive processes, namely, thinking, is an activity that is inferred to be going on when an individual is engaged in solving problems, which also involves the use of models. Thinking is also inferred to be going on when an individual simply "scans" his own memories or perceptions. Hallucinogenic drugs such as PCP can cause these thoughts to be elaborated into fantasies, dreams, and hallucinations.

Thoughts of PCP-intoxicated subjects are usually short, confused, wandering, rapidly changing, and unvolitional in nature. The intoxicated individual experiences waves of such thoughts interrupted by waves of blank (amnesic) periods. The rapidly accelerated thinking itself, coupled with the drug-induced hyperexcitability and euphoria, can lead to the clinical condition called "flight of ideas" or "mania."

The most common thoughts during intoxication concern changes in body image. Each individual normally develops techniques for integrating the feelings and experiences emanating from his/her body. This is referred to as body image, body concept, or body scheme. 'The PCP-intoxicated individual has difficulty in experiencing and organizing his/her body as a perceptual object. Individuals become so unaware of their bodies that they often feel free of them and have the sensation of floating out of them. They often float back and forth into and out of their bodies. When they do perceive their bodies, their thoughts contain exaggerated and elaborated views such as inflated limbs, changes in head size, difficulty in estimating size of body parts, difficulty in estimating distance between body parts, and a general tendency to <u>overestimate</u> body size and height. While such subjective reactions have not been confirmed experimentally, they are similar to those findings reported for the hallucinogen LSD (Fisher 1970).

Frequently, the intoxicated individual considers himself/herself endowed with unique and superior abilities (both bodily abilities and mental abilities) as a result of the thought changes. In the extreme cases, this state can be manifested as paranoia, whereby the subject tries to account for these thought disturbances with persecutory or grandiose delusions.

THINKING ABOUT DEATH

Intense hallucinogenic experiences, including PCP experiences, can be regarded as journeys to new states of consciousness (Lear-y, Metzner, and Alpert 1964). The characteristic features are "the transcendence of verbal concepts, of space-time dimensions, and of the ego or identity" (p. 11). The journey has been described as one resembling psychological death and many similarities between hallucinogenic experiences and those of dying patients have been noted (Grof and Halifax 1977). There are also considerable similarities between PCP intoxications and death experiences.

Domino and Luby (1972) describe a salient feature of PCP intoxication as reduced verbal productivity, the appearance of calm in the subjects, and reported experiences of sheer "nothingness." One subject reported lying in a meadow and that "this meadow was a place that he has often considered he would like to be buried in. The theme of death ran through most of his retrospective account of the episode. Possibly the experience of combined cut-off of interoceptive and exteroceptive cues is close to one's conception of what death must be like" (p.42).

Other common deathlike experiences in PCP intoxications include ineffability of the experience and difficulty in verbal behavior; feelings of peace and quiet; disturbances in space and time perception; out-of-body phenomena (including ecstatic feelings of timelessness, weightlessness, peace, serenity, and tranquility); no perception of smells, odors, temperature, or kinaesthesia; fear; and confusion. Naturally, this can lead to a concern with death and deathlike thoughts for the PCP-intoxicated individual. This state of preoccupation with death has been termed *meditatio mortis.*

It is well known that survivors of near death situations developed, as a result of such experiences, new concepts about death. Many of these individuals lost their fear of death and developed positive attitudes toward it. Indeed, it is this observation that forms the basis for much of the recent psychotherapy with hallucinogenic compounds for terminal patients. However, it must be emphasized that these positive changes in attitudes about death are not associated with a desire for death or with suicidal tendencies. Nonetheless, it may be speculated that in the acutely intoxicated PCP user, such attitudes may function to remove or reduce fear in situations which risk extreme bodily harm or death.

AGGRESSION AND CRIMINAL BEHAVIOR

A variety of factors contribute to the development of aggression and criminal tendencies. Many of these can be understood in terms of social psychological concepts: frustrations creating an emotional arousal predisposing to aggressive behavior; aggressiveness habits also predisposing to such behavior; external cues evoking the hostile actions; and, disinhibition of socially disapproved responses (Berkowitz 1962).

PCP intoxication can produce frustration by interfering with a person's ongoing goal-directed activity, arousing anger, and thus leading to aggressive reactions if suitable aggression cues (stimuli associated with the frustrater) are present. Even if such cues are not present in reality but simply inferred by the user to be present due to hallucinations and/or thought disorders (e.g., paranoia state), the individual may display relatively uncontrolled, intense emotional responses. These intense reactions to real or imagined frustrations predispose him/her to extremely hostile behavior. However, the predisposition to aggression is not manifested necessarily by aggressive behavior *per se,* and this depends on individual personality, social, and cultural factors. Nonetheless, given the presence of the hostility-evoking cues as found in police encounters or in criminal activities where resistance is encountered (as in robbery or rape), violent aggressive behaviors are more likely to be elicited from the user.

Chronic use of PCP may induce a poor judgement syndrome which could be a factor in nonviolent criminal acts such as perjury and theft. The hypersexuality sometimes reported during some psychotic stages of PCP intoxication may influence motivation involved in assault and rape situations. Conversely, one could speculate that crime related to continuous use of drugs (e.g., theft to support the drug habit) would be infrequent among PCP users owing to the drug's low price and availability. In addition, like most hallucinogens, PCP does not appear to be used in escalating doses indicative of addiction.

PCP intoxication also can produce panic reactions in the sense that the individual becomes frightened due to the overwhelmingly intense hallucinogenic effects. Changes in body image, perceptual distortions, and mental confusion can catapult the naive user into a state where s/he feels and fears loss of ego and identity, loss of contact with reality, and even permanent mental dysfunction. Consequently, panic ensues, and deviant behavior, including aggression, can occur. It is probable that assaultive behavior, when it does occur during PCP intoxication, takes place for many individuals at this time. This is similar to the occurrence of aggressive behaviors during intoxication with other hallucinogens: "Aggressive outbursts do occur during the panic reaction of psychedelic intoxication, especially if the reaction includes paranoid components" (Tinklenberg 1973, p.265).

The PCP-intoxicated user's orientation toward the immediate present and disregard for long range consequences of his/her behavior would make it difficult for him/her to premeditate criminal acts. But the tendency to react strongly to sensory stimuli in the immediate environment, the inclination to refer everything to oneself that often develops into paranoia, and the need to do something due to intense psychomotor stimulation can all produce an aggression-prone individual. Once again it must be emphasized that emotionally stable people under the influence of low doses of PCP probably will not act in a way very different from their normal behavior. To the extent that this is true, case histories and statistics regarding PCP-related crime, aggression, and violence should thoroughly investigate the user's prior conduct and social psychological history.

THE DIMINISHED CAPACITY DEFENSE

Forensic psychopharmacologists and psychiatrists are frequently called upon as expert witnesses in cases involving PCP and diminished capacity. The expert will frequently evaluate several sources of data regarding the defendant's possible state of intoxication at the time of the alleged offense. These sources include: chemical and laboratory reports and studies, field sobriety tests, observations made by arresting officers, arrest reports, investigative reports, statements of witnesses, medical and psychiatric histories, and allied materials. According to Pollack (1976), the expert "must be able to assess, integrate, and evaluate all of these data on the question of whether the defendant at the time of the alleged act was intoxicated; and if he was, whether his mental functions of significance for forming the specific intent for the crime were substantially impaired" (p. 257) . Thus, the threshold for simply being intoxicated or under the influence of a drug such as PCP is significantly lower than that defining intoxication for purposes of diminished capacity. The former requires minimal evidence of impairment while the latter requires a substantial degree of mental impairment. In an effort to gather as much information as possible, experts will frequently employ additional data such as physical medical examination of the defendant soon after the alleged offense, EEG examinations, in-depth interviewing and testing of defendants and witnesses regarding the specific phenomenology of the intoxication, among other methods. All such materials can be used as collateral and supporting data. Since there is no statutory presumption identifying PCP intoxication for diminished capacity (in contrast to the statutory presumption of being under the influence of alcohol with blood alcohol levels of .10 percent), the expert witness can only offer considered opinion. In court, when accepted according to the rules of evidence, psychopharmacologic or psychiatric expert opinion carries weight as "opinion evidence" and is not accepted as "scientific fact." The ultimate legal question will be decided by the trier of fact, namely, the judge or jury.

Since PCP intoxication <u>can</u> resemble closely some forms of schizophrenia, superficially it would appear to be an ideal candidate for defenses of diminished capacity. PCP intoxication can show all the essential ingredients for such a defense: altered consciousness wherein the defendant's attention, awareness, and ability to respond meaningfully to the environment and situation are disturbed; mental confusion regarding the meaning of the act or its consequences; involuntary behavior which might prevent optional courses of action; and interference with goal-directed behavior so as to prevent organizing and directing physical movements. Thus, PCP can diminish the capacity to form or to harbor criminal intent. It does so by interfering with the mental functions which are essential to the mental process of forming intent for an act.

Diminished capacity defenses are extremely difficult to prove and are generally far less successful than the insanity defense, which is probably successful in about 66 percent of the insanity trials. Even when the diminished capacity defense is successful, the outcome may not result in the adequate treatment of the defendant for the drug abuse and mental health problems signified by such extreme PCP use. Whereas the defendant who is found legally insane is usually diverted to a state mental health system for evaluation, disposition, and treatment, the defendant who 'is successful in a diminished capacity defense is usually committed to prison for punishment.

OVERVIEW AND SPECULATIONS

Euripides presented us with the notion that drugs work in some magical way. The figure of Dionysus was clearly that of sorcerer and his magic was to be found in wine. The social importance of Dionysian intoxication and ecstasy was that it permitted temporary impairment of reason for the folly and madness of criminal behavior. Ever since those ancient times, drugs, and especially alcohol, have been used as scapegoats for the argument of diminished capacity in criminal acts. The mechanisms of action for such effects are neither magical nor predictable. They are not magical because they reflect characteristic states of behavior induced by the pharmacological properties of drugs on the central nervous system. They are not predictable because of a wide range of interactions with nondrug variables, including set and setting.

Phencyclidine is not a magical drug. It does not magically produce violent, assaultive, or criminal behavior. When the psychopharmacology of the drug is fully appreciated, we can begin to understand that the criminal behavior associated with its use is a result of interactions between the drug and the user. At that time the magical notions will begin to disappear from courtroom trials of diminished capacity which often turn into trials of the drugs themselves as good or evil.

Such a future state of enhanced knowledge about drugs has already been envisioned by science fiction writer H.H. Hollis (1972) in his short story "Stoned Counsel." In that fictitious world of the future, hallucinogenic drugs have become a routine part of the legal process as both defense attorneys and prosecutors have had personal experiences with drugs which enhance their understanding and sympathy for the defendants. Even some present day PCP users have coined the term "Pig Killer" for the drug in order to connote that if ingested by police it would kill their ideas about the drug turning people into "beasts." While such personal use is unnecessary and certainly ill-advised with drugs such as PCP, a full understanding of phencyclidine will undoubtedly reveal it to be simply a hallucinogenic drug with certain chemical properties and behavioral possibilities.

ACKNOWLEDGMENTS

The author thanks Dr. Murray E. Jarvik for numerous helpful services in the research and preparation of this study. The author is indebted to Ada Hirschman for superlative research assistance.

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Chapter 17

Control of Drug Self-Administration: The Role of Aversive Consequences

Nancy K. Mello, Ph.D.

Despite a continuing search for commonalities across the various forms of substance abuse, it has been difficult to identify factors which apply equally to the abuse of opiates, alcohol, stimulants and hallucinogens. The traditional focus on specific syndromes associated with the abuse of certain drugs, e.g., alcoholism and heroin addiction, has tended to militate against appreciation of similarities between drugs. Moreover, known differences in the pharmacological and behavioral consequences of alcohol, heroin, cocaine and phencyclidine intoxication would appear to argue against the notion that any meaningful similarities could be found.

Re-examination of the behavioral consequences of drug use and abuse suggest that one pervasive factor has often been overlooked. Many drugs of abuse have now been shown to have aversive consequences during intoxication. These data have led to the hypothesis that "aversive" consequences may be an important factor in the control of many forms of drug abuse (Mello 1977). Recent findings relevant to this hypothesis will be examined in the remainder of this review. One basic assumption is that drug self-administration behavior is controlled or maintained by its consequences. Therefore, any consistent consequence which transcends drug specific effects may be a common factor which contributes to the maintenance of substance abuse.

EFFECTS OF DRUGS IN NAIVE USERS

In thinking about the way in which drugs come to control behavior leading to their self-administration, it is instruct-' ive to review some reported effects of acute drug use by naive users. It would be convenient if the initial drug experience was so overwhelmingly positive that repeated drug use would be almost inevitable. Yet the reported effects of acute doses of opiates, barbiturates, alcohol and nicotine summarized in Table 1 do not appear to be especially appealing. These drugs each produce a variety of somatic and emotional effects that would seem disadvantageous to the user. Yet, despite these "aversive" consequences of initial drug use, many individuals persist in self-administration of these same drugs to the point of abuse and addiction.

TABLE 1

SOME REPORTED ACUTE EFFECTS OF DRUGS IN NAIVE USERS*

	OPIATES	BARBITURATES	ALCOHOL	NICOTINE
NAUSEA	X		X	X
VOMITING	X		X	X
DIZZINESS	X			X
SWEATING				X
DYSPHORIA	X	X	X	
EMOTIONAL LABILITY		X	X	
AGGRESSIVITY			X	
IMPAIRMENTS IN:				
CONCENTRATION	X	X	X	
THINKING	X	X	X	
COMPREHENSION		X	X	
MEMORY		X	X	
JUDGMENT		X	X	
DROWSINESS	X	X	X	
LETHARGY	X	X	X	

**From Mello, Stimulus Self-administration: Some implications for the prediction of drug abuse liability. In: Thompson and Unna, eds.* Predicting Dependence Liability of Stimulant and Depressant Drugs. *© 1977 University Park Press, Baltimore. Reprinted with permission. Adapted from Jaffe 1975, Mello and Mendelson 1976, Russell 1976.*

It has often been observed that alcohol addicts tend to have a clear recollection of their "first drink" (Kuehnle, Anderson, and Chandler 1974). However, clinical impressions suggest that the first drink was not memorable because of its relaxing, euphorigenic, tension-reducing, or self-actualizing effects for the drinker (Kuehnle, Anderson, and Chandler 1974; Catanzaro 1968). It is more likely that the future alcoholic drank to the point of intoxication with associated despondency, nausea and vomiting.

The process by which an initial aversive drug experience becomes translated into a repetitive drug use pattern is not understood. It could be postulated that with the development of drug tolerance, these seemingly unpleasant somatic and emotional effects undergo a transition to a more positive state, i.e., euphoria, relaxation, tranquility. Alternatively, it could be postulated that the initial dysphoria, nausea, and vomiting is an integral part of the reinforcing properties of subsequent drug abuse. It is now evident that drug abuse is maintained despite the recurrence of these seemingly aversive consequences.

EFFECTS OF DRUGS IN CHRONIC USERS

It is generally acknowledged that the long-term effects of chronic substance abuse are adverse and may compromise health and employability as well as disrupting family and social relationships. However, the immediate consequences of drug use are usually believed to be sufficiently positive to outweigh these long-term effects. If in fact, abused drugs consistently produced relaxation, euphoria, relief from anxiety, tranquility and serenity, then chronic drug use and abuse might be more understandable. However, common expectancies about drug related pleasures have not been confirmed in clinical studies of addicts during intoxication. Direct observations of intoxicated individuals are often discordant with retrospective self-reports of drug effects obtained during a period of sobriety. This discrepancy is particularly troublesome since most of our information about the effects of abused drugs is based on retrospective reports of users during sobriety.

It now appears that increases in dysphoria, anxiety, and agitation frequently accompany chronic intoxication, both with alcohol (Mello and Mendelson 1978) and with heroin (Mirin et al. 1976; Meyer and Mirin 1978). These findings challenge the traditional view of the behavioral effects of these drugs, and are one basis for the idea that “aversive” consequences are important in the maintenance of drug self-administration behavior. Clinical research has shown that the behavioral effects of drugs are far more complex than concepts related to hedonism would suggest.

Behavioral Effects of Alcohol Intoxication

Many of the consequences of alcohol intoxication are similar for the naive or social drinker, and for the alcohol addict. The major determinant of the behavioral effects of alcohol appears to be the dose of alcohol consumed, relative to the experience and behavioral tolerance of the drinker. A list of some of the subjective states that alcohol is believed to improve or enhance, and findings from clinical studies of intoxicated individuals appears in Table 2.

Low doses of alcohol, sufficient to produce a blood alcohol level of between 30 and 50 mg/100 ml often produce the anticipated pleasurable consequences. However, social drinkers report increased depression, dysphoria and anxiety after an acute high dose of alcohol (6 to 8 ounces) (Williams 1966; Warren and Raynes 1972).

Alcohol addicts often ingest between 26 and 32 ounces of distilled spirits per day (or the equivalent in beer or wine) (Mello and Mendelson 1978). Since the alcoholic is tolerant to alcohol, considerably higher doses of alcohol may be required to produce significant changes across a range of subjective experiences and interpersonal reactivity. However, clinical studies from many laboratories, employing a variety of techniques agree that chronic intoxication, sufficient to maintain blood alcohol levels between 150 and 300 mg/100 ml, is associated with increased depression, agitation, anxiety, and belligerence in the drinker (Mello and Mendelson 1978). Severe chronic alcohol intoxication may also be associated with illusions and hallucinatory experiences during drinking as well as during alcohol withdrawal (Wolin and Mello 1973).

TABLE 2

OBSERVED EFFECTS OF ALCOHOL INTOXICATION*

	LOW DOSE	HIGH DOSE
MOOD	↑	↓
ANXIETY	↓	↑
DEPRESSION	↓	↑
SOCIABILITY	↑	↓
SELF-IMAGE	↑	↓
SEXUALITY	↑↓	↑↓
RELAXATION	↑	↓
FANTASY-REVERIE	↑	↑
SLEEP	↓	↓

**Adapted from Mello and Mendelson 1978.*

It is not clear why the discrepancies between the expected and the observed effects of chronic alcohol intoxication are not more generally recognized and why they appear to have so little effect on the behavior of the alcohol addict. It has been found that alcohol addicts, interviewed before, during, and after an episode of alcohol intoxication tend to recall pre-drinking expectancies about the experience even if these are completely at variance with the actual effects of alcohol intoxication (McGuire et al. 1966). Alternatively, it may be that these "aversive" consequences, similar to the "first drink" experience summarized in Table 1, are an important aspect of the reinforcement for drinking.

Behavioral Effects of Heroin Intoxication

Retrospective reports of the effects of heroin intoxication by heroin addicts emphasize euphoria and serenity. As Jaffe (1975) has described it:

> Narcotics do more than produce indifference to pain. They also suppress those drives that motivate an individual to appease hunger, seek sexual gratification and respond to provocation with anger. In short, they seem to produce a state of total drive satiation. Nothing needs to be done because all things are as they should be. For certain types of personalities, but clearly not for all, such a state is extremely pleasant (Jaffe 1975, p. 284).

Clinical observations of heroin addicts during a period of opiate intoxication are at variance with these reports. Chronic opiate use appears to be accompanied by an increase in dysphoria, irritability, hypochondriasis, psychopathology, belligerence, negativism and motor retardation (Wikler 1952; Haertzen and Hooks 1969; Mirin et al. 1976; Meyer and Mirin 1978). These dysphoric consequences of chronic heroin intoxication appear to be directly related to heroin use rather than to situational or social factors. Heroin addicts, maintained on the long-acting opiate antagonist, naltrexone, during the same period of residence on a clinical research ward did not develop dysphoria, anxiety, or belligerence comparable to that shown by heroin users (Mirin et al. 1976; Meyer and Mirin 1978).

It could be argued that a brief and transient positive mood change which is purportedly associated with the induction of alcohol and heroin intoxication is sufficient to maintain drug self-administration behavior (Mirin et al. 1976; Davis 1971). In the case of alcohol intoxication, these initial changes during the induction of intoxication have been difficult to characterize either in terms of subjective quality or temporal duration (Davis 1971). In the case of heroin addiction, the intensity of the positive feelings associated with the rush appears to be attenuated as tolerance develops during the course of chronic heroin use (Meyer and Mirin 1978).

Comparisons with Phencyclidine

Clinical reports of the consequences of phencyclidine self-administration appear to be a further extension of the "aversive" end of the drug effect continuum. Acute effects of dose-related illusions, dissociation, perceptual disturbance, and depersonalization, which may culminate in convulsions and coma would be difficult to categorize as "positive" effects according to the usual criteria. Yet even the development of toxic psychosis does not appear to be an effective deterrent to repeated use. However, re-evaluation of the consequences of alcohol and opiate intoxication suggests that phencyclidine abuse may differ only in the intensity of aversive effects.

ANIMAL MODELS OF "AVERSIVE" STIMULUS SELF-ADMINISTRATION

Although it is tempting to dismiss these clinical data as optimistic expectancies failed, the quest for aversive stimulation is not restricted to man. There is evidence that seemingly aversive consequences will also maintain self-administration behavior in animals under certain conditions. Two examples of aversive stimulus self-administration will be described.

Narcotic Antagonist Self-Administration

Narcotic antagonists induce withdrawal signs in opiate dependent monkeys. A summary of some typical withdrawal signs appears in Table 3. It is evident that the somatic consequences of opiate withdrawal resemble some consequences of acute intoxication in naive drug users shown in Table 1. It is not surprising that opiate-dependent monkeys will work to escape and to avoid the infusion of narcotic antagonists (Downs and Woods 1975; Hoffmeister and Wuttke 1973). However, it has also been found that under certain conditions morphine dependent monkeys will work to produce injections of narcotic antagonists.

TABLE 3

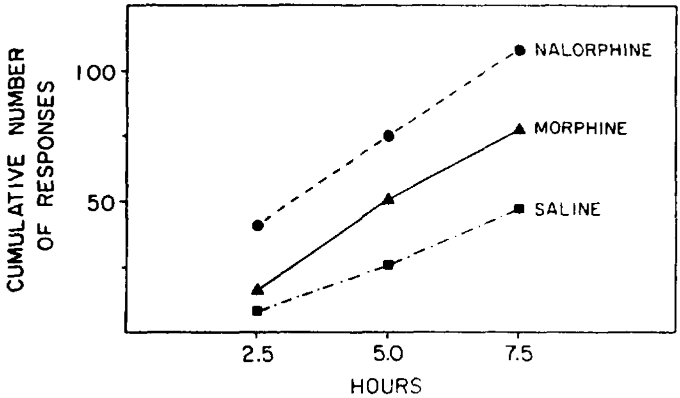
SOME SIGNS OF OPIATE WITHDRAWAL IN OPIATE-DEPENDENT RHESUS MONKEYS*

Autonomic and Gastrointestinal Signs	Motor Activity Signs
Vomiting	Tremors
Retching	Rigidity in extremities
Coughing	Spasticity
Tachypnea	Shivering
Dyspnea	Piloerection
Salivation	Holding of abdomen
Sweating	Gross Behavioral Changes
Tearing	Yawning and grimacing
Miosis	Restlessness
Erection & Masturbation	Screaming (provoked and unprovoked)
Loose stools	Attacking [provoked and unprovoked)

**Adapted from Villarreal and Karbowski 1974.*

Goldberg and co-workers (1972) were the first to observe self-administration of the narcotic antagonist nalorphine by opiate-dependent monkeys. During studies in which either saline or nalorphine was substituted for morphine injections during a 7.5 hour session, it was found that responding that was followed by nalorphine injections was maintained at a higher rate than responding that was followed by saline injections. The distribution of responses within successive 2.5 hour segments of the 7.5 hour saline and nalorphine substitution sessions is shown in Figure 1. It is apparent that nalorphine maintained responding. Monkeys continued to self-administer nalorphine despite severe withdrawal signs which included vomiting? coughing, salivation, tremors, and irritability. Responding for nalorphine did not extinguish during the substitution sessions.

FIGURE 1



Distribution of responses within the last three saline substitution sessions and nalorphine-substitution sessions (100 mcg/kg injection), compared to the distribution of morphine-maintained responses at comparable times on control days. Abscissa: successive 2.5-hour segments of 7.5-hour saline or nalorphine substitution sessions; Ordinate: cummulative number of responses during successive 2.5-hour segments. Each point represents the mean of results of three sessions with two monkeys. From: Goldberg, S.R., Hoffmeister, F., Schlichting, U.U.: Morphine antagonists : Modification of behavioral effects by morphine dependence. In: J.M. Singh, L. Miller and H. Lal eds. <u>Drug Addiction I. Experimental Pharmacology</u>, pp. 31-48. ©1972, Symposia Specialists, P.O. Box 610397, Miami, Florida 33161. Reprinted with permission of the publisher.

These data indicate that under certain conditions, response produced nalorphine injections can maintain responding in monkeys which are physiologically dependent upon morphine. Goldberg and co-workers concluded that these findings illustrate that the experimental history of the organism, and the behavioral schedule under which a stimulus event is presented, rather than the type of event may determine the effect that an event may have upon behavior (Goldberg, Hoffmeister, and Schlichting 1972).

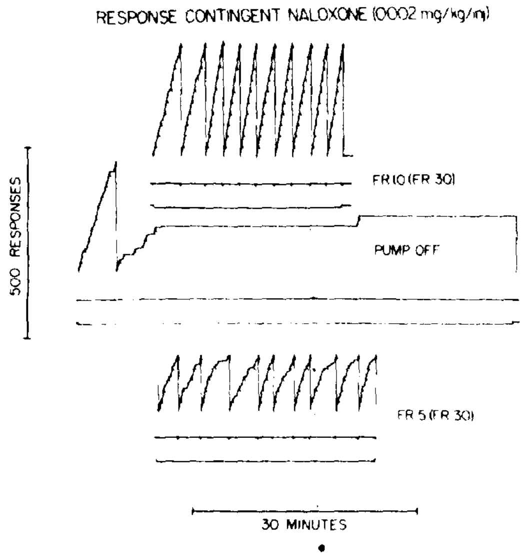
These findings have recently been confirmed and extended by Woods and co-workers (Woods, Downs, and Carney 1975). It was found that under certain conditions, morphine dependent monkeys will work to produce the same injection of a narcotic antagonist, naloxone, that they previously worked to avoid. Cumulative records of narcotic antagonist self-administration by a morphine dependent monkey is shown in Figure 2. Each response on an operant manipulandum advances the stepping pen of the cumulative recorder approximately one-quarter of a millimeter and consequently, cumulative records provide a direct analog of response rate. The top row of figure 2 show cumulative records of responding on a second-order schedule of reinforcement (FR 10 (FR30:S). Every 30 responses produced a secondary reinforcing stimulus (i.e., a 1.5 second flash of light), previously associated with drug infusion and every three hundred responses produced an injection of naloxone (0.002 mg/kg). Antagonist injections were followed by a one-minute time out and a light signal. The downward deflection on the event marker indicates the delivery of each successive naloxone injection.

It is clear that naloxone, rather than any associated stimuli maintained responding since removal of naloxone resulted in extinction of response behavior. The second row of Figure 2 shows the effect of disconnecting the naloxone infusion pump when the secondary reinforcing stimuli, i.e., the light signal, the time-out, etc., remain unchanged. The monkey worked briefly, then stopped responding when no naloxone infusion was delivered. The third row of Figure 2 illustrates the reinstatement of naloxone maintained responding during the first session after the naloxone pump was reconnected. The reinforcement schedule requirement was reduced from 300 to 150 responses for each naloxone injection. Under these conditions, morphine dependent monkeys could earn approximately 10 naloxone injections over the course of an hour. It is apparent that the monkey resumed and maintained responding for naloxone injections.

ELECTRIC SHOCK SELF-ADMINISTRATION

The aversive properties of electric shock stimuli have been amply documented. However, it has also been found that the same electric shock event that can maintain escape and avoidance behavior, may under certain conditions, be self-administered by the same monkey. Identification of this phenomena, called response-produced shock, developed from the initial observations of Kelleher and co-workers that during a pre-shock stimulus, responding increased and if the terminal shock was removed, responding decreased (Kelleher, Riddle, and Cook 1963). Response produced shock

FIGURE 2



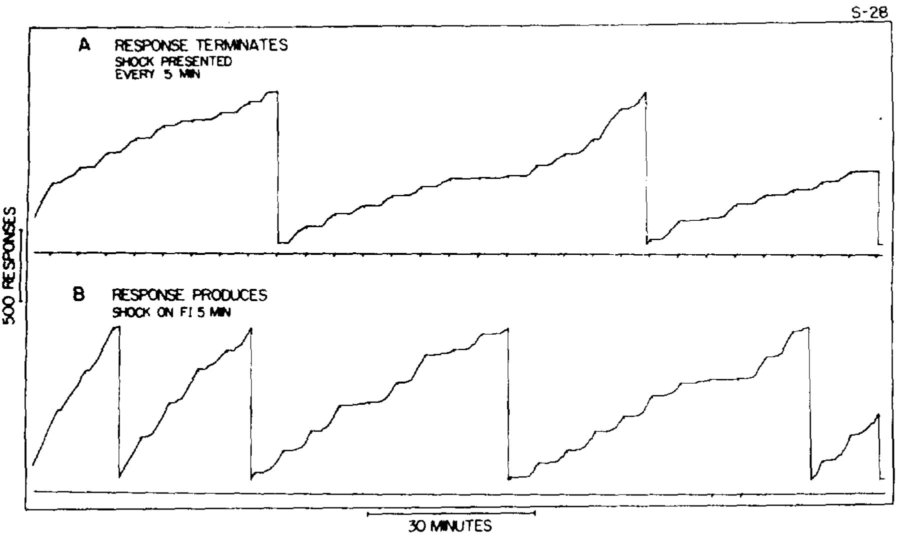
Cumulative records of responding maintained by naloxone in a morphine-dependent monkey. The upper record shows the eighth session of responding when every completed FR 30 unit produced a 1.5~sec flash of the house light and every tenth completed FR 30 unit produced an injection of naloxone (0.002 mg/kg per injection) plus a 1-min time-out accompanied by house light illumination. The center record shows performance in the third session with the naloxone infusion pump disconnected. All other aspects of the procedure were as described above. The lower record shows reinstatement of naloxone-maintained responding in the first session with the naloxone pump reconnected. In this and subsequent sessions, the schedule value was reduced to FR 5 (FR 30). Injections of naloxone or saline are indicated by downward deflections of the center event pen. Each session was terminated after 10 injections or about 1 hour. From Woods, J.H., Downs, D.A., and Carney, J. 1975. Behavioral functions of narcotic antagonists: Response drug contingencies. Reprinted with permission of the publisher, from FEDERATION PROCEEDINGS 34(9): 1777-1784, 1975.

has now been observed in many laboratories, across several species, and has been shown to be a reliable and persistent phenomena (Byrd 1969; Eubanks et al. 1975; Kelleher and Morse 1968; McKearney 1968, 1969, 1972; Morse and Kelleher 1970; Morse, McKearney, and Kelleher 1977; Morse, Mead, and Kelleher 1967; Stretch, Orloff, and Dalrymple 1968; Stretch, Orloff, and Gerber 1970). Under certain conditions monkeys will continue to self-administer electric shock for months and even for years.

An illustration of behavior maintained by the delivery of electric shock is shown in Figure 3 (Morse and Kelleher 1970). Cumulative response records of the operant performance of a single monkey are shown under two different conditions; shock termination and shock production. The top row of Figure 3 shows behavior on a schedule of shock termination (FI 5 min) in which the first response after five minutes have elapsed terminates a 7 ma electric shock which is presented every five minutes. Cumulative responses of the same monkey on a schedule of shock production are shown in the second row of Figure 3. Instead of terminating a shock presented every five minutes, the monkey self-administers a shock of 1 ma every five minutes, If a response did not produce shock within five seconds after elapse of the five minute fixed interval, a 7 ma shock was presented automatically. It is obvious that the rate of responding was higher when responses produce shock than when responses terminate shock.

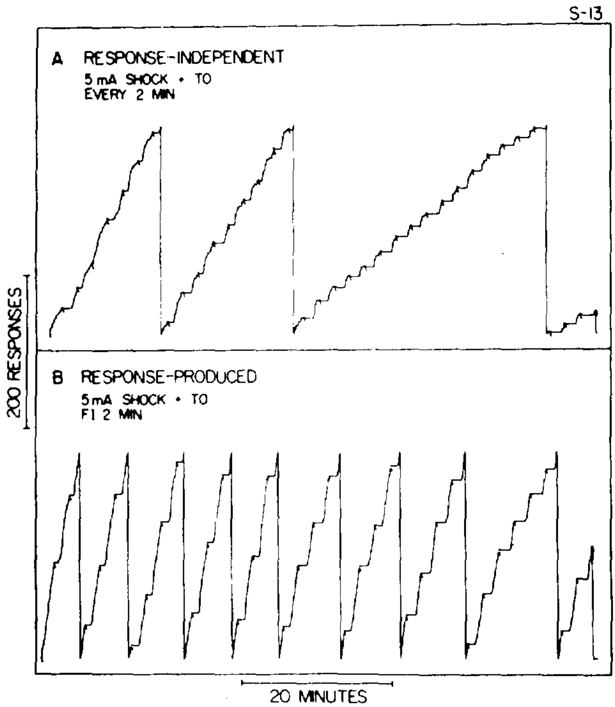
Another example of response-produced electric shock is shown in Figure 4 which compares the effects of non-contingent and response produced shock on operant behavior (Morse and Kelleher 1970). In the cumulative record shown at the top of Figure 4, a monkey with a particular behavioral history received 5 ma shocks every two minutes, independent of his response behavior, Each shock was followed by a brief time-out period. In the lower portion of Figure 4, a shock of the same intensity (5 ma) was scheduled to occur after the first response after an interval of two minutes had elapsed (an FI 2 min schedule), Shock presentation was followed by a brief time-out. Response behavior was maintained by electric shock presentation. The rate of responding increased and the pattern of responding was more positively accelerated on a shock presentation schedule than when shocks were not contingent on responding. These findings that an animal will work to self-administer a seemingly noxious electric shock, indeed the same electric shock he previously worked to avoid, or to escape from is eloquent testimony to the capacity of "aversive" events to control behavior leading to their self-administration. Morse, McKearney, and Kelleher (1977) have reviewed data on the control of behavior by noxious stimuli and discussed the generality of this phenomenon.

FIGURE 3



Performance under an FI 5 min schedule of termination of electric shock and an FI 5 min schedule of presentation of electric shock (Monkey S-28). A: Short diagonal strokes in the event record (bottom) indicate successive electric shock presentations (7 ma); diagonal strokes on the cumulative record (top) indicate the termination of shock. B: Strokes on the cumulative record indicate 1 ma electric shock presentations. If a response did not produce shock within 5 seconds after 5 minutes had elapsed, a 7 ma shock was presented automatically. When responses produced shock, rates of responding became higher and patterns of positively accelerated responding became more marked. From Morse, W.H., and Kelleher, R.T., 1970. Schedules as fundamental determinants of behavior. In: W. N. Schoenfeld, ed. The Theory of Reinforcement Schedules. pp. 139-185. Appleton-Century-Crofts, New York. © 1970. Reproduced by permission of Prentice-Hall, Inc., Englewood Cliffs, New Jersey.

FIGURE 4



Comparison of performances under schedules of response-independent and response-dependent 5-ma electric shocks (Monkey S-13). Short diagonal strokes on the cumulative records indicate presentation of electric shock; a time-out period, in which the paper did not moue, followed each shock. The recording pen reset to the baseline whenever 275 responses had accumulated. A: Performance under the schedules of response-independent shock. B: Performance wader FI 2-min schedule of response produced shock after eight sessions. The rate of responding increased, and the pattern of responding was more clearly positively accelerated with response-produced shocks. From Morse, W.H., and Kelleher, R.T., 1970. Schedules as fundamental determinants of behavior. In: W. N. Schoenfeld (ed.) . <u>The Theory of Reinforcement Schedules</u>, pp. 139-185. Appleton-Century-Crofts, New York. © 1970. Reprinted by permission of Prentice-Hall, Inc., Englewood Cliffs, New, Jersey.

The parallels between these data on response-produced shock and narcotic antagonist self-administration in primates, and the aversive consequences of drug self-administration in humans are provocative. Although the control of drug self-administration by aversive consequences has not been shown unequivocally in man with the degree of precision that it has been shown in primate models, the inference that aversive consequences are one part of the reinforcement complex that maintains human drug self-administration behavior is compelling.

IMPLICATIONS AND CONCLUSIONS

These clinical and experimental data challenge common sense assumptions about what constitutes a "positive" and an "aversive" event, and what types of events will be reinforcing. In the language of the experimental analysis of behavior, reinforcement is any event that maintains behavior, i.e., a reinforcer is a consequence of behavior that increases the probability of the recurrence of that behavior (Skinner 1938, 1953). Although behavioral scientists are usually careful to distinguish between reinforcement and reward, the terms reinforcing, rewarding, and euphorigenic are often used interchangeably to describe the consequences of drug abuse and by inference to explain its recurrence and persistence. The notion of "reward" has a compelling face validity that does not invite critical examination. One advantage of the term reinforcement is that it does not imply anything about the nature of the reinforcing events, but rather describes a functional relationship between events and behavior.

The defining characteristics of reinforcements and punishers are how they change behavior. The same stimulus may have either reinforcing or punishing effects, depending upon the condition under which it is presented. According to this empirical formulation, shown schematically in Table 4, if the presentation or removal of the stimulus event <u>increases</u> the behavior leading to that consequence, it can be defined as a reinforcer. If the presentation or removal of the stimulus event <u>decreases</u> the behavior leading to that consequence, it can be defined as a punisher (Morse and Kelleher 1977).

TABLE 4

EVENT	BEHAVIORAL EFFECT *	
	INCREASE BEHAVIOR	DECREASE BEHAVIOR
PRESENT STIMULUS	REINFORCEMENT	PUNISHMENT
REMOVE STIMULUS	REINFORCEMENT	PUNISHMENT

**From Mello, Stimulus self-administration: Some implications for the prediction of drug abuse liability. In: Thompson and Unna, eds. Predicting Dependence Liability of Stimulant and Depressant Drugs.*

Defining stimulus events in terms of their behavioral effects, rather than in terms of an apriori assumption about the alleged properties of the stimulus event and conclusions about its consequences, represents a radical departure from our usual ways of thinking. However, a definition of reinforcement and punishment in terms of behavioral effects, can account for data on response-produced shock and antagonist self-administration as well as the persistence of drug self-administration which results in aversive consequences during intoxication.

Electric shock and antagonist self-administration data indicate that it is not the inherent properties of the event, per se, but the way in which the event is scheduled that determines the subsequent effect on behavior (Morse, McKearney and Kelleher 1977). The reinforcing or punishing properties of stimulus events are dependent upon a variety of factors including the behavioral history of the organism, the schedule of presentation of that event, and the ongoing behavior at the time. Clearly, it is impossible to assume an invariant effect of any particular Stimulus event. We have seen that under certain conditions of behavioral history and schedule controls, substances that were so noxious that animals would work to avoid them, undergo a transition from punishing to reinforcing stimuli as a function of the schedule of presentation.

Since consequences which appear to be aversive do maintain behavior leading to their self-administration, more careful attention to the role of "aversive" consequences in human drug self-administration seems indicated. Traditional concepts that drug abuse is maintained primarily as a function of rewarding or euphorigenic consequences are not consistent with the clinical data. Reward related concepts appear too limited to account for clinically observed consequences of many forms of drug abuse including phencyclidine self-administration.

Stimulus Self-Administration ?

Beyond the issue that both seemingly "aversive" and "positive" consequences contribute to the maintenance of drug self-administration, there are many other apparent paradoxes which remain unaccounted for. One example is polydrug use which often involves the simultaneous and sequential use of several drugs with different pharmacological properties and presumably different effects, e.g. stimulants and depressants; opiate analgesics and stimulants. Phencyclidine may be used concurrently with other drugs, e.g. alcohol, barbiturates, marihuana, each of which has different pharmacological effects and presumably modulates the effect of phencyclidine in different ways.

Twenty-five years ago, Wikler and Rasor (1953) wrote that one reason for using drugs advanced by some opiate addicts is to "get off the normal". The nature of the positive effects of drugs described by addicts varies considerably in different types of drug addiction (Wikler and Rasor 1953). Anecdotal accounts of voracious polydrug use, and extreme drug effects produced by agents such as phencyclidine, suggest that the users goal is to achieve a rapid change in state. The direction of the change, up or down, may be of secondary importance. Accumulating clinical evidence of aversive consequences during intoxication also lends credence to a state change hypothesis. An extreme example is the repeated intravenous injection of phencyclidine to the point of unconsciousness (Fauman and Fauman 1978).

To the extent that stimulus change affected by drug use may be more important than any inherently positive or negative characteristics of that stimulus, it may be useful to consider drug self-administration within a more general framework of stimulus self-administration (Mello 1977). Central to the idea that stimulus self-administration is important in the maintenance of drug self-administration is the notion that the stimulus properties of drugs, rather than the specific qualities of the stimuli, may be important determinants of this behavior. State change may be the subjective response to the drug induced stimulus, whatever that stimulus may be. Perhaps, under some conditions, in individuals with a certain behavioral history, drug self-administration has less to do with the pharmacological properties of the compound, or with its anticipated effects, than with its properties as a definite stimulus event that results in a change in subjective state. This hypothesis implies that any drug which has definite stimulus properties, i.e., behavioral effects for the user, is a drug which has abuse potential.

ACKNOWLEDGMENTS

Preparation of this review was supported by grants DA 01676 and DA 4RG010 from the National Institute of Drug Abuse, ADAMHA. Portions of this paper have been adapted from "Stimulus Self-Administration: Some Implications for the Prediction of Drug Abuse Liability" by N.K. Mello, 1977.

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