The potent psychotomimetic agent phencyclidine, 1-(1-phenylcyclohexyl) piperidine (PCP), is currently found in numerous street drug preparations. But unlike most other recreational drugs, PCP cannot be accurately placed in a definite category such as hallucinogen (LSD), depressant (Quaalude® or stimulant (amphetamine), for, depending on the individual using PCP and the dose taken, any one or all three of these effects may occur (Petersen & Stillman 1978). The use of PCP (popularly known as “angel dust,” “angel’s mist,” “hog,” “the PeaCo pill” and “T”) is common in the drug community (Rainey & Crowder 1974; Hart, McChesney & Grief 1972; Lindgren et al. 1969).

In addition to the sale of PCP as PCP, it is also being sold to the unwary buyer as LSD, cocaine, mescaline and psilocybin, but most frequently as the psychoactive component of marijuana – tetrahydrocannabinol (THC) (Garey et al. 1979; Lundberg, Gupta & Montgomery 1976). The smoking of PCP sprinkled on a marijuana cigarette has become a popular method for obtaining what has been described as a “high exceeded only by that obtained with cocaine” (Garey et al. 1979; Boyd 1974). This mixture, empirically derived by drug users, appears to have a scientific basis. Recent findings have demonstrated that Δ9-THC, the principal psychoactive component of marijuana, potentiates the effects of PCP (Murray & Craighill 1976). The increasing use of PCP, its nefarious sales as other compounds and the “spiking” of other street drugs such as cocaine or heroin with PCP has resulted in dramatic increases in the number of PCP overdoses encountered by medical communities, law enforcement agencies and coroners’ offices. A better understanding of this drug would, therefore, benefit not only those who use it, but those who are responsible for the medical, legal and forensic management of its toxic effects.

SYNTHESIS AND CHEMICAL PROPERTIES

The synthesis of PCP involves the use of benzene, piperidine and p-toluenesulfonic acid. Additionally, ether, cyclohexanone, phenol-Mg-Br, isopropyl alcohol, hydrochloric acid, ammonium chloride, ammonium hydroxide and phenol-lithium are used at various stages of its preparation (Maddox, Godefroi & Parell 1965). The failure to remove these toxic compounds from the final preparation appears to have been responsible for some of the severe physiological effects such as abdominal cramps, blood emesis, convulsions, coma and

![Phencyclidine]

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death as sometimes seen with the ingestion of PCP (Burns et al. 1975). Presently, however, with more sophisticated laboratory equipment, improved chemical knowledge and new solvents for distillation, a relatively pure (99%+) preparation can be achieved and the toxic effects of impurities eliminated or reduced (Lerner & Burns 1978).

Since the pure base of PCP is highly insoluble in water, it is rarely seen on the streets. Rather, PCP is usually prepared as the readily soluble hydrochloride salt. The final product appears as a white granular powder which is freely soluble in water and ethanol. When sold on the streets, however, it may appear in any color (e.g., white, red, tan, blue, green) and in any form (e.g., tablet, crystals, powder, liquid) (Lerner & Burns 1978). Therefore, on the basis of either color or form, PCP is difficult if not impossible to detect without laboratory assistance. If one is aware of the solubility differences between THC and PCP, however, it becomes quite simple to distinguish between them, as both are soluble in ethanol, but only PCP is soluble in water.  

Pure PCP has a molecular weight of 243.88 and a melting point of 234-236°C. It is a relatively stable compound, both in the crystallized form or in solution. In addition to PCP, at least 30 analogs have been synthesized, many of which appear to have psychoactive properties. Of these 30-plus compounds, four have been identified in street drug operations, TCP (thiophene analog), PCE (N-ethyl analog), PIP (phenylecyclohexyl pyralidene) and PCC (pyridocyclohexane-carbonitrile) and as the race between the street chemists and the law enforcement agencies goes on, most, if not all, of the 30-plus analogs will have made an appearance on the streets in one guise or another (Domino 1978).

PREVALENCE

The use of PCP as a street drug, either alone or in combination with amphetamine, cocaine, mescaline, LSD or marijuana, has been confirmed by numerous studies in which street drug samples were analyzed. PCP, for example, was detected in 184 of 237 samples submitted to the Department of Chemistry at Kansas University between August, 1970 and January, 1972 (Hart, McChesney & Grief 1972). During another two-month period, PCP was detected in 195 samples submitted for analysis (Anonymous 1973); in Philadelphia, PCP was found in eight of 20 samples of “mescaline” (Schnoll & Vogel 1971). In Massachusetts, 10 of 20 drug samples analyzed contained PCP (Linden, Lovejoy & Costello 1975).

Since 1975, however, only 25 percent of the street drugs analyzed for PCP have contained additional drugs. This figure is down from the 40 to 60 percent of drugs previously found to contain PCP plus one or more other drugs. A California study found that LSD was the drug most often mixed with PCP, representing 86 percent of the mixtures analyzed. Cocaine and PCP and marijuana and PCP combinations were found in only four percent or less of the samples tested (Lerner & Burns 1978). However, in New Orleans about 40 percent of patients presenting with symptoms of PCP toxicity have reported that their PCP was mixed with marijuana and that they purchased this mixture as “Superweed” but were unaware who had mixed it (Garey et al. 1979). The incidence of PCP and cocaine mixtures is steadily increasing and this combination is apparently sold on the street as pure, high grade cocaine to the naive buyer (Garey et al. 1979; Lerner & Burns 1978). The reason for this particular combination is apparently financial since a small amount of cocaine mixed with 2-5 mg of PCP will yield a larger profit. Several samples of heroin confiscated in the New Orleans area were also shown to contain PCP. Perhaps the strangest combination seen, however, was that of PCP and peanut butter which was sold on the street in both an edible and injectable form.

As could be readily predicted, the widespread use of phencyclidine, either knowingly or unknowingly, has increased the number of overdoses reported in the medical literature. The frequency of such overdoses has prompted reports suggesting that “PCP abuse has become so increasingly common that PCP toxicity should be considered in patients with unexplained acute psychosis, dystonic reactions, status epilepticus or coma” (Tong et al. 1975). It was reported that between the fall of 1973 and the spring of 1974, 11 male patients were admitted to a Washington, D.C. hospital suffering from PCP-induced psychosis. These admissions resulted in a report at the American Psychiatric Association meeting entitled, “Epidemic of Psychosis Caused by Use of Angel’s Dust” (Luisada & Reddick 1975). Numerous other examples of one or multiple cases of PCP overdose can be found in current medical literature (Fauman et al. 1976; Luisada & Brown 1976; Linden, Lovejoy & Costello 1975; Tong et al. 1975). The admission of 11 patients suffering from PCP psychosis in 1974-75 was considered at that time an epidemic. At Charity Hospital of New Orleans between April 1, 1978 and March 31, 1979, approximately 210 cases of PCP intoxication were seen in the emergency room and 13 more were detected in the coroner’s office (Garey et al. 1979). What was once considered to be epidemic numbers in a year is now less than what is seen in a month. Add to this the fact that only a fraction of the requests for PCP determination on overtly psychotic or behaviorally
deranged patients are screened by adequate laboratory methods, and the possible number of cases could easily quadruple.

Some recent reports on PCP use throughout the country suggest that PCP is a drug of the white middle classes with minorities frequently underrepresented (DeAngelis & Goldstein 1978; Lerner & Burns 1978). This fact, however, appears to be an artifact of where and how the sample population was obtained and the numerical ratio of majority to minority subjects in that particular area (Fauman & Fauman 1978). In New Orleans, for example, the ratio of black to white overdose patients seen in local emergency rooms and who were proven to have taken PCP was 58:48 percent which was for all purposes identical to the black:white ratio in the city, 55:45 percent. From this finding it would appear that PCP is a drug that is used regardless of race or socioeconomic status (Garey et al. 1979).

Lerner and Burns (1978) reported that for the first 11 months of 1977, PCP was identified in drug samples obtained from 28 states and that the criminal element involved with the distribution of heroin is now distributing and selling PCP. The reasons behind the increasing use of PCP as a recreational drug and the involvement of the “organized” criminal element in its sale and distribution are numerous and are related to the facts that: 1) it is relatively easy and inexpensive to synthesize and yields a high profit margin; 2) it can be snorted, injected, eaten or smoked and, therefore, can be easily sold as other compounds; 3) it can be mixed with cheap low-grade marijuana and sold as “Superweed” or used to cut cocaine or heroin, thereby dramatically increasing the potential profits; and 4) it produces a “good” trip in approximately 80 percent of first time users.

HISTORY

The search for an efficient intravenous anesthetic led to a series of cyclohexylamine derivatives being synthesized and studied in the laboratory. The first of these was PCP, which was marketed by Parke, Davis and Company in 1963 under the name Sernyl®.

The use of PCP as an anesthetic in surgical procedures in humans, although generally effective, was discontinued due to the occurrence of unpleasant side effects. Some patients experienced extreme excitement, visual disturbances and delirium upon emerging from PCP-induced anesthesia. During preliminary animal studies, it was observed that during surgery the animal had its eyes open and looked about unconcernedly (Greifenstein et al. 1958). This blockade of sensory input and lack of profound physiological effects on other systems suggested that PCP works almost exclusively on the nervous system and, in particular, on the higher sensory integrative functions of the central nervous system (CNS). It was hypothesized that PCP and its derivatives produced a blocking effect of sensory input without concomitant sleep and without significant depression of respiration and circulation. The biochemical and pharmacological properties of PCP tend to support this hypothesis.

Other therapeutic investigations of phencyclidine focused on its potential as an analgesic (pain killer) and its use in research in and treatment of mental disorders. Parke-Davis, in a letter to the Food and Drug Administration on January 22, 1965, requested that further human clinical investigations be discontinued, however, because of problems with bizarre adverse effects. In early 1967, phencyclidine became commercially available again as Sernylan®, marketed for “veterinary use only.” In 1969 Bio-Ceutic Laboratories, Inc. acquired the production rights to Sernylan® but as of April 1, 1979 all legal manufacturing of PCP in this country ceased, and at present the Federal Government is the only legitimate source of PCP in the United States.

PCP first appeared on the street in 1967 in San Francisco. However, due to the side effects already noted by the clinical testers of the drug, PCP’s popularity was short-lived. It disappeared from the streets in early 1968 only to reappear on the street in the early 1970s. At this time its popularity climbed until it took its present place among the five most commonly used street drugs.

PRECLINICAL STUDIES

PCP has been shown to affect the catabolism, steady-state levels and turnover rates of most of the putative neurotransmitters in the CNS. Although Ban (1969) has classified PCP as an anticholinergic agent, Maavyani et al. (1973) have shown that it is a competitive inhibitor of acetylcholinesterase (AChE). The psychotomimetic effects of PCP, however, appear to be more closely related to its anticholinergic effects than its ability to block AChE activity. Additionally, in the peripheral nervous system, PCP blocks the reuptake of norepinephrine (NE) into postganglionic nerve terminals and has anticholinergic properties at muscarinic receptors (Nedergaard 1973; Weinstein et al. 1973). Other studies involving the central nervous system have demonstrated that PCP affects the metabolism of serotonin (5-HT), NE and dopamine (DA) which are the major putative neurotransmitters and which are thought to be intimately involved with the expression of emotion and other various behavioral and motor functions.
controlled by the brain. Although some of the effects reported for PCP on neurotransmitter metabolism can be questioned on the grounds of species specificity or inadequate experimental design (Johnson 1978), one neurochemical aspect of PCP is of particular interest — its dopaminergic properties. Specifically, the properties of PCP such as the ability to competitively inhibit the uptake of dopamine into presynaptic terminals, to cause the spontaneous release of dopamine from nerve ending particles (Smith et al. 1977; Garey & Heath 1976) and to stimulate tyrosine hydroxylase and DA sensitive adenylate cyclase activity are all properties which would tend to increase DA activity in the brain (Garey et al. 1977). When related to several current hypotheses and clinically observable conditions, this potent dopaminergic activity may be the single most important neurochemical property of PCP. For example, the dopamine hypothesis of schizophrenia is presently the most widely accepted theory used to explain the biochemical etiology of schizophrenia (Tammenga et al. 1977; Snyder et al. 1974). Since acute psychotic reactions caused by PCP closely resemble those of acute schizophrenic episodes, it is possible that both have the same or a similar neurochemical basis. Additionally, schizophrenic patients given PCP have exacerbations of the primary symptoms of their disease which they cannot distinguish as being drug induced (Luby et al. 1959). This subject will be discussed further in the clinical studies section. Another line of evidence linking PCP reactions to DA activity is in its pharmacological similarity to amphetamine. Amphetamine, like PCP, increases the release and inhibits the reuptake of DA and clinically can induce a psychosis that closely resembles paranoid schizophrenia (Janowsky et al. 1973; Angrist & Gershon 1969). However, amphetamine psychosis is induced only with the prolonged use of amphetamines and is rarely seen after single doses, unlike the psychosis induced by PCP. In animals both amphetamine and PCP have stimulatory effects in certain behavioral paradigms which are postulated to be caused by excessive DA activity. In rats that have been unilaterally lesioned in the substantia nigra, for example, ipsilateral turning behavior is elicited by both amphetamine and PCP. This type of turning is potentiated by cholinomimetics, reduced by anticholinergics and blocked by DA blocking agents such as haloperidol, a potent antipsychotic agent (Fessler, Sturgeon & Meltzer 1979; Finnegan, Kanner & Meltzer 1976). PCP also has been shown to potentiate the effects of amphetamine in experiments designed to measure stereotyped behavior. This type of behavior is utilized as an experimental model for human psychosis and is also used to screen compounds for antipsychotic activity (Balster & Chait 1978). Again, this effect can be blocked by DA blocking agents which are also clinically effective antipsychotic compounds (Murray 1978). As pointed out by most researchers, however, there is a qualitative difference between the effects of PCP and amphetamine in such animal experiments. This difference can be explained in several ways: 1) the more potent anticholinergic effects of PCP as compared to amphetamine; 2) the ability of PCP to competitively inhibit 5-HT reuptake; and 3) the ability of PCP to bind to the opiate receptors in brain tissue, a property which amphetamine does not have (Vincent et al. 1978). Given the wide spectrum of CNS activity that PCP possesses, it is reasonable to speculate that the diverse physiological and psychological response of the nervous system to PCP is a result of complex interactions with numerous neurotransmitter systems both in the central and peripheral nervous system. However, the compelling, if circumstantial, evidence supporting the DA theory of schizophrenia, the potent dopaminergic properties of PCP and the similarity of functional and PCP-induced psychosis strongly suggests that excessive DA activity may be the common factor in the induction of both of these conditions. Additionally, an extension of the DA model for acute schizophrenic states has postulated that psychosis can arise from an imbalance of the cholinergic and dopaminergic systems in the brain involved with the control of emotional expression (Friedhoff & Alpert 1973). Again, the potent dopaminergic properties of PCP, in addition to its anticholinergic and cholinomimetic activity, would tend to support such a model. Both models, however, are based on excessive activity of the DA systems which are involved with controlling the expression of emotional and behavioral manifestations of a complex nervous system. The overstimulation of these systems by PCP may provide a working model to study the biochemical basis not only of drug-induced psychosis but for the functional psychoses as well.

In the CNS there are several pathways consisting of DA-containing neurons. One of these, the mesolimbic pathway, is believed to be involved with emotions and behavioral expression and is, perhaps, the one on which PCP is acting to induce the psychosis seen so often with the use of this drug. Another pathway which contains predominantly DA neurons is the nigrostriatal system. If the hypothesis concerning the DA basis for PCP psychosis is correct, then PCP should also affect the nigrostriatal pathway which is intimately involved with motor activity and coordination. Diseases of this pathway which, theoretically, would increase DA activity are thought to be responsible for Huntington's Chorea, tardive dyskinesia and drug-
induced dyskinesia (Carroll, Curtis & Kikmen 1977; Smith et al. 1977). Numerous animal experiments in which such abnormal movements are elicited by excessive DA activity have been performed. The abnormal (e.g., ataxic, dyskinetic and choreiform) movements seen in the above mentioned clinical disease states and those seen in certain animal experiments are similar to those observed with toxic PCP reactions. Again these types of movement disorders are postulated to have as a basis excessive DA activity but in pathways in the brain that function to control movement (nigrostriatal) rather than behavior (mesolimbic). The similarities, therefore, between PCP-induced and functional psychosis and between PCP-induced movement disorders and clinical disease states exhibiting a similar type of disorder is compelling evidence that PCP affects the basic processes controlling not only movement but the expression of both emotions and behavioral patterns.

**CLINICAL STUDIES**

In 1958 Greifenstein investigated Sernyl® as a human anesthetic and reported that at doses of more than 0.5 mg/kg I.V., the patients became agitated; at 1 mg/kg rigidity occurred, followed by catatonia and convulsions. A dosage of .25 mg/kg was found to be satisfactory for anesthetic use and was used in 34 patients undergoing surgical procedures. During the procedure, the majority of patients were quiet, but several became agitated and confused, although this may have been related to inadequate analgesia. Other effects included: 1) elevation of blood pressure in all, with some patients having an accompanying increased heart rate – hypotension and bradycardia were not observed; 2) muscle relaxation was not achieved and in some cases increased muscle tone and hyperactive deep tendon reflexes were observed; 3) vertical and horizontal nystagmus; 4) bilateral paresis with impaired pupillary reactivity; 5) increased minute and tidal respiratory volume; 6) impaired visual identification; 7) pin prick was appreciated but was no longer painful and other sensory modalities were also decreased (e.g., the impairment of proprioception was perhaps responsible for the ataxia); 8) EEG was characterized by diffuse slow wave pattern with suppression of the fast activity as contrasted to barbiturate in which fast (beta) rhythm is accentuated.

Post-operatively, the patients were initially dissociated and euphoric, their behavior resembling alcohol intoxication. This lasted three to 19 hours following the operation. Not infrequently, the patients had violent emergence reactions during which they became agitated and combative. These states were successfully treated with meperidine or morphine. When their attention and consciousness cleared, they had retrograde and antegrade amnesia, although awake in the operating and recovery rooms. For up to 24 hours, the patients complained of dizziness with true rotational component and nystagmus. Because of these reactions, the use of Sernyl® in anesthesia was discontinued in humans and was used only as an anesthetic in primates. Other derivatives of this group, such as cyclohexamine, were also tried in humans, but again, severe psychological postoperative disturbances were noted.

Davies and Beech, in 1960, administered Sernyl® to 12 normal volunteers (0.75 mg/kg) and reported that, unlike LSD, the acute effects of PCP began almost immediately and were over within an hour, although general malaise persisted for several hours. No hallucinations were reported, unlike LSD or mescaline, but dramatic changes in perception (i.e., distortion of body image, depersonalization, disruption of time perception and slowness and/or difficulty in concentration or remembrance) were seen. These investigators suggested that these symptoms were similar to certain primary symptoms of schizophrenia and, therefore, might have a similar basis. In normal volunteers, the following psychological and psychomotor parameters were altered following PCP administration: 1) decreased speed in performing rapid repetitive motor tasks, including tapping a stylus upon a motor plate for a 10 second period; 2) lowered rate of flicker to perceived visual fusion; 3) poor estimation of time interval; and 4) decreased immediate recall and concreteness of thought in proverb interpretation. Physical findings which occurred included decreased proprioception, pain and temperature discrimination, pupillary dilation with decreased reactivity, horizontal and vertical nystagmus, increased tone and tendon reflexes with clonus, but no Babinski sign, fine sustentation tremor, dry mouth and lips.

In other studies (Ban 1969; Ban, Lohrenz & Lehmann 1961; Luby et al. 1959) PCP was administered to normals as well as schizophrenics. Both groups reported similar findings — the activations of primary symptoms of schizophrenia to a greater degree than either mescaline or LSD. The drug did not normally produce hallucinations. Patients with chronic schizophrenia appeared to be highly resistant to LSD and mescaline and were able to tell the difference between the effects of these two drugs and the symptoms of their illness. In contrast, PCP exaggerated their associative defect and frequently their inappropriate affectivity. It also resulted in feelings which were more characteristic of the acute and earlier stages of schizophrenia.
changes lasted for weeks and suggest that PCP may act upon some fundamental aspect of this disease. Distortion of body images and an intense fear of dying were the more characteristic symptoms observed, the same as reported for normal volunteers receiving this drug. Therefore, the use of PCP in treating psychiatric illness, particularly schizophrenia, was not and cannot be recommended under any circumstances. From the foregoing studies several conclusions can be made: 1) PCP can induce a psychosis that is clinically indistinguishable from schizophrenia; 2) the psychotomimetic effects of PCP are most frequently seen when low doses of the drug are taken, such as the amount taken in street preparations; 3) acute psychotic reactions are most frequently seen in young adult males; 4) chronic schizophrenics receiving PCP will experience an acute exacerbation of their psychosis which may last up to six weeks; 5) the only use of PCP in relation to human subjects is that of a research tool to study the neurochemical events which trigger the schizophrenic-like psychosis that PCP can induce. Because of moral, legal and ethical restraints, the clinical and/or laboratory administration of PCP to human subjects for research purposes has for all intents and purposes been stopped since 1972. The explosive use of PCP as a "recreational drug," however, has turned its street use into one gigantic experiment without the benefits of scientific control or management.

MEDICAL FINDINGS

In reviewing the cases seen during the course of our study and those reported in the literature, a wide variety of symptomatology emerges which appears to be dependent on: 1) social setting; 2) dose level and route of administration; 3) other drug involvement; and 4) personality traits. Behavioral anomalies most frequently reported are agitation, anxiety, disordered thought processes, body image disturbance, euphoria, depersonalization and, occasionally, auditory and/or visual hallucinations. Agitation is frequently seen following diminution of the acute symptoms. The prevalence of visual hallucinations is much less frequent with PCP than with other drugs known to cause a toxic delirium; those that are reported are more suggestive of an illusionary state related to the body image disturbance rather than to true hallucinations. Auditory hallucinations, however, occur quite frequently and usually take the form of an intensification of a sound in the immediate environment, at times to the exclusion of all other sounds. For this reason, any attempts to talk to these patients is usually nonproductive until this "exclusion of sounds" has been alleviated (Stein 1973).

It was originally reported that in cases of PCP-induced psychosis, there is minimal paranoid ideation and the patient is not anxious, combative or hostile. If these are present, an underlying psychiatric disorder or mixed drug reaction should be suspected. These original reports, however, do not appear to be valid as the number of cases identified increases. For example, in at least 48 percent of the cases reported in a recent study, violence was the outstanding symptom with hostility and agitation reported almost as frequently (40 percent). In none of these cases were other psychoactive, sedative, stimulant or hypnotic drugs detected. Luisada and Brown (1976) described phencyclidine psychosis in the more severely affected users and considered this to consist of three phases: 1) initial violent psychotic behavior with prominent paranoid ideation, lasting up to one week; 2) restless and combative delirium without violence for one week; and 3) rapid personality reintegration and restoration of normal thought processes and associations. We have recently modified these findings and have suggested that the following description may be more appropriate: 1) initial violent, aggressive and/or disorganized behavior with or without paranoid ideation lasting from less than four hours to as long as several days; 2) restless and combative behavior for 24 to 48 hours but in some cases lasting up to seven days; and finally 3) personality reintegration and restoration of normal behavioral and thought patterns usually complete in one week but in severe cases requiring 12 to 18 months to return to predrug status (Garey et al. 1979). Whether in cases which require prolonged treatment or hospitalization the drug has precipitated a latent psychosis is not clear, but this is a possibility that should be considered and will be discussed in more detail later. Neurological symptoms that occur in some but not all patients are nystagmus (rotary, horizontal, vertical), variable pupil size with depressed light reflex, diminished pain and temperature response, ataxia, slurred speech, tremors, increased deep tendon reflexes, clonus and muscle weakness. At higher doses, dystonic reactions, including opisthotonic posturing, torticollis and facial grimacing have occurred. At doses which approach or exceed the anesthetic level, respiratory depression, coma, decreased muscle tone and status epilepticus have been reported. In some instances this has led directly to death (Burns et al. 1975). It is important to point out, however, that as laboratory and diagnostic criteria for identifying PCP psychosis are improved, the number of patients presenting with psychiatric symptoms will far outweigh those presenting with medical problems. As stated previously, the psychotomimetic effects of PCP are predominant with
exposure to low doses of the drug. As the dosage taken is increased, the medical symptoms will appear and overlap with the behavioral ones. As the dose is increased even further the psychosis or behavioral disruptions will disappear and major medical crises will predominate. Occasionally, as a patient emerges from a coma or seizure and as the blood level of PCP becomes sufficiently reduced, an emergence reaction such as violent, hostile or psychotic behavior will appear, reminiscent of those reported following surgical procedures involving PCP as an anesthetic.

As an anesthetic, PCP appears to block selected sensory inputs such as pain. However, PCP administered to volunteer subjects in isolation chambers results in a feeling of “utter nothingness.” Upon emergence from the chamber, distorted perception, prolonged reaction time and marked depression of the proprioceptive senses occurred, but the psychological disturbances previously noted were absent or greatly reduced (Cohen et al. 1960). It appears, therefore, that exteroceptive input is required to produce the psychotomimetic effects seen with PCP. Another factor which suggests that the exteroceptive input is important in the symptomatology of PCP is that attempts to “talk down” a bad PCP trip may cause intensification of the symptoms (Stein 1973; Cohen et al. 1960). In examining these findings, it could be hypothesized that, after an initial anesthetic effect, even if subclinical, the exteroceptive sensory inputs to the CNS become “supersensitive” and the ability of the person to process incoming signals is grossly impaired and/or distorted. This inability to adequately interpret exteroceptive inputs may be responsible for the overt psychotomimetic effects observed clinically.

Other factors such as age, sex and personality also appear to function in the production of psychotomimetic symptoms following PCP usage. Young adult males appear to be more susceptible than females or older age groups (Johnstone, Evans & Bugel 1959). At anesthetic doses, not all patients became psychotic or displayed behavioral problems. In fact, only about 10 to 20 percent displayed these symptoms, even after anesthetic doses. Several reports have shown that the disinhibitory potential of PCP and the activation of the psychopathology results in the quiet, undertaker person becoming supercorous and catatonic, and the overactive person becoming agitated and restless (Gershon & Olariu 1960; Greifenstein et al. 1958). This intensification of underlying personality traits is comparable to the reported intensification of primary symptoms (i.e., inappropriate affect and associated defects) in schizophrenics given PCP. Apparently, the drug tends to amplify the basic processes determining the mental status of the user.

Another facet of PCP intoxication that is becoming more apparent is the “recycling” or flashback effects. In approximately 20 percent of the cases reported, behavioral and/or medical symptoms may appear, resolve and then reappear for up to 30 days after a single dose of PCP and without apparent reexposure to PCP or any other psychoactive drug (Garey et al. 1979; Fauman & Fauman 1978; Lerner & Burns 1978). This presents a difficult problem not only to the medical community, but also to the patients, for in many of these cases, the patients are treated and released from the hospital only to return within 24 to 48 hours, usually in police custody for violent or bizarre behavior or abortive suicide attempts. In several documented cases, outbursts of violent psychotic behavior following a single dose of PCP were shown to occur over a 30 to 40 day period. These outbursts always coincided with the reappearance of PCP in the urine of these patients and in the periods between these episodes, negative reports for urinary PCP were obtained (Garey et al. 1979). This recycling or flashback effect appears to be related to the chemical properties of this compound. PCP is a weak base with a PKa of 8.5. Since normal physiological pH is 7.2, the majority of PCP will tend to be deionized in the spinal fluid, blood or urine. In the deionized form PCP is difficult for the body to clear since it is readily reabsorbed (Aronow & Done 1976; Done et al. 1975). For example, as PCP is passed from the enterohepatic circulation into the strongly acidic milieu of the stomach it will ionize. This prevents its reabsorption into the blood. As it leaves the gut, however, and the pH rises, the PCP molecule will deionize which in turn enhances its reabsorption into the blood and hence its recirculation through the body. This chemical property of PCP is, in all likelihood, responsible for its recycling effect and is also the basis for specific medical treatment which will be discussed later.

The various reports dealing with the incidence of acute psychotic behavior following the administration of PCP, whether as a surgical anesthesia or as a recreational drug, seem to indicate that about 15 to 20 percent of those taking the drug will have a “bad trip” (Lerner & Burns 1978). This finding coupled with the fact that young adult males are more susceptible to its effects strongly suggests that the possibility of adverse reactions to PCP may be related to a genetic factor. There is compelling evidence that schizophrenia has a strong genetic component; therefore, it is possible that persons who experience acute psychotic reactions to PCP may be genetically predisposed to schizophrenia or other severe mental illnesses and that PCP is precipitating what is in
effect a true schizophrenic or depressive episode. As previously mentioned, PCP is devastating in its ability to exacerbate the primary symptoms of schizophrenia in chronic sufferers of this disease. When these facts are considered as a whole, the idea that PCP may be precipitating a true psychotic episode in a latent schizophrenic is a reasonable possibility. The PCP user should be aware, therefore, that if a family history of severe mental illness (e.g., schizophrenia, depression) exists, one would be taking a great risk to use PCP as a recreational drug because the odds of inducing a true psychotic state appear to be very high.

From several cases we have followed and from more numerous cases reported in the literature, we have observed that chronic PCP users must be followed closely by competent psychiatric personnel because they apparently have a strong tendency to become deeply depressed. This state may, within a short period of time, lead to suicide or attempted suicide (Garey et al. 1979; Lerner & Burns 1978). As Lerner and Burns (1978) have pointed out, chronic PCP use apparently develops from the “downer” feeling the user gets when a previous trip is wearing off. To compensate for this feeling the patient then takes more PCP to get “high” again and this pattern is repeated until a pattern of chronic abuse has been established. At some point the users become socially withdrawn, and this withdrawal may be followed by severe depression which could lead to suicidal thought and may ultimately lead to self-destruction.

TREATMENT

Because PCP is rapidly absorbed, removal by lavage or with emetic is usually unsuccessful. Recently, removal of PCP by continuous gastric drainage following acidification of the urine or blood by ammonium chloride has been suggested in severe cases (Arnow & Done 1976; Done 1975). The combination of PCP with other drugs makes the management of overdoses a critical problem. Fatal status epilepticus has been reported in which both PCP and barbiturates were found (Kessler et al. 1974). This combination can also lead to respiratory collapse. Warnings have been issued not to use phenothiazines in treatment of overdoses, since the drug combination may have contained belladonna, which would lead to an atropine (anticholinergic) crisis, which would then require treatment with 2-4 mg physostigmine (Taylor, Maurer & Tinklenberg 1960). To compound the problem in such cases, the anticholinergic effect of the phenothiazine may cause hypotension and bradycardia. In cases where PCP is known to be the only drug involved, chlorpromazine (CPZ) is claimed to be an effective antidote by some, while others feel that, although CPZ is beneficial, PCP-induced psychosis does not respond to CPZ as quickly as schizophrenia (Balster & Chait 1976; Luisada & Reddick 1975). Haloperidol has been suggested as the drug of choice in treating PCP psychosis since it modifies the psychosis with less chance of inducing an atropine crisis in the event of anticholinergic involvement (Gershon & Olariu 1960). A problem that one must be aware of, however, is that PCP may cause dystonic reactions which may be exacerbated by haloperidol. Succinate has also been suggested as an antidote to PCP, but reports on this treatment have been conflicting (Neubauer, Sundland & Gershon 1966; Gershon & Olariu 1960). With the multiple properties of PCP, it is possible that no single drug will be effective in treating all symptoms seen in cases of PCP overdose. At the present time, supportive medical care, a quiet but reassuring environment, diazepam (Valium®) to reduce increased muscle tone (spasticity) and opisthotonus, Benadryl® for the dystonic reaction and Haldol® for the acute psychotic reactions are suggested. Begin psychiatric intervention only after the agitated state is controlled and the patient is clinically stable. It has been recently suggested that Inderal® (propranolol) be used to control the physiological effects of a possible “dopamine storm” precipitated by PCP. The use of Inderal® may be helpful from this standpoint but apparently does little if anything to ameliorate the behavioral problem (Rappolt, Gay & Farris 1979).

As previously mentioned, the combination of PCP and barbiturates may well prove fatal. Several deaths from the use of this mixture have been reported and are due, most likely, to the additive effects of two depressant compounds producing respiratory arrest. Consequently, barbiturates should not be used to control seizures induced by PCP as this combination may lead to respiratory arrest as easily in the hospital as on the streets. We have observed two cases of such an effect but fortunately they occurred in a hospital where emergency medical assistance was available and hence both patients recovered. This pointedly demonstrated the potential lethal effects of barbiturates and PCP. The procedure of choice for treating PCP-induced seizures appears to be: Valium® followed by Dilantin® if Valium® does not suffice and finally by a Paraldehyde® drip if the two previous agents are ineffective.

LABORATORY DIAGNOSIS

The use of routine laboratory drug screening procedures with a sensitivity of 1µg/ml or greater will not detect approximately 90 percent of cases involving PCP (Garey et al. 1979). In order to adequately detect the presence of PCP in body fluids, a sensitivity in the
range of 5-50 ng/ml is required to identify 80-90 percent of the samples containing PCP. Either gas chromatograph-mass spectrometry or gas chromatograph with a nitrogen-phosphorous detector are required to adequately ensure identification of PCP in the large majority of patients. This is especially true when few if any medical symptoms are present and behavioral disturbances or acute psychosis are the primary presenting symptoms. In general, patients that have urinary levels of PCP that can be detected by routine laboratory methods have numerous accompanying physical symptoms that aid in the diagnosis of PCP toxicity. In fact, many of these cases present with trauma, seizures or coma and the behavioral problems, if present, are secondary in nature.

Urine is the specimen of choice for detecting PCP in most patients. Blood levels may be too low for even the more sensitive analytical techniques and of little value if routine methods are to be used. Even if 72 hours have elapsed since the patient was exposed to PCP it is still possible to detect the drug in urine samples. Furthermore, in some cases the drug can still be detected seven days after exposure.

SUMMARY

The steady rise in the promiscuous use of phencyclidine (PCP) as a “recreational” drug has recently gained nationwide attention because of the numerous violent and/or bizarre incidents caused by the use of this drug. Because the media often exaggerate reports of bizarre and violent behavior to make a “good” story, the potential PCP user may be tempted to ignore the media warnings. In the case of PCP, however exaggerated the story, a real danger does exist. So, despite numerous newspaper, radio and television warnings about the possible consequences of PCP use and abuse, the incidence of toxic reactions continues to climb.

In many cases PCP is sold as other drugs, particularly THC, and in various colored capsules, tablets, liquids and crystals which may explain the increased usage despite the numerous warnings against its use. The advances in laboratory techniques and chemical processes have enabled the clandestine chemist to prepare relatively pure PCP and thus eliminate many of the toxic side effects due to impurities in the drug. In addition, 30 or more psychoactive PCP analogues have been developed and are starting to make an appearance on the street.

PCP is perhaps the most potent psychotomimetic compound known at the present time and is capable of inducing a psychosis which is clinically indistinguishable from schizophrenia. The psychosis-producing effects of PCP are the most common toxic effects seen in hospital emergency rooms; but as the amount of PCP taken and/or the simultaneous involvement of other drugs, particularly barbiturates, occurs, severe medical problems (e.g., coma, seizures, respiratory arrest) begin to appear. Death from high doses of PCP or PCP plus other drugs does occur, but the principal cause of death from PCP abuse is due to trauma, homicide or suicide (usually of the bizarre or violent form). Young adult males, persons predisposed to mental illness and naive drug users appear to be the most susceptible to the adverse effects of PCP. The fact that chronic PCP users are starting to increase in number is mute testimony that not all users experience “bad trips” with PCP. Unfortunately for the user, however, this does not guarantee that the next trip will not be a bad one. The effects of chronic use seem to be twofold: severe depression with suicidal thoughts and numerous violent, agitated behavioral patterns. Neither seems to be a suitable alternative.

At the present time there is no specific antidote for toxic PCP reactions and the prolonged psychosis induced in some cases does not appear to respond to the standard antipsychotic medications as quickly as do the functional psychoses. The major improvement from a medical standpoint is the development of more sensitive laboratory techniques to confirm the presence of PCP in body fluids. This advance has undoubtedly led to the apparent increase in the number of PCP cases reported by hospitals and to the accuracy of clinical diagnosis by medical, drug or law enforcement communities.

In a review article written three years ago, the statement was made that in a sense PCP is a much more dangerous drug than the “hard” narcotics. This opinion can, of course, be debated. However, with the increasing incidence of heart-rending occurrences, needless fatalities and bizarre suicides attributed to persons under the influence of PCP, this statement appears to be more true today than it was three years ago. PCP was, and is now, the most dangerous compound to ever be accepted on the streets as a recreational drug and until the drug community accepts this fact, the litany of murders, suicides, violent crimes and broken lives will continue to escalate.

NOTE

1. THC is a highly unstable compound which must be treated with extreme care if it is to retain its viability. For this reason THC is never found on the street.
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REFERENCES


Epidemic of X (2):


