

PCP: From Surgical Anesthetic to Schizophrenic Mice

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Phencyclidine, known widely as PCP, has a colorful history. Drug researchers at Park-Davis pharmaceutical company in the 1950s noted that this newly created chemical caused a “drunken state” in rats, “canine delirium”, as well as some very odd behavior in pigeons. After being sold as a general anesthetic for surgery in humans, it was soon recalled. Upon waking from surgery, patients frequently experienced such effects as agitation, psychosis, and bizarre distortions of body image. After the recall for human use, PCP had a brief life as a veterinary tranquilizer before legal manufacturing was almost completely outlawed in 1979. This was partially because PCP is easy to make in clandestine laboratories, however, PCP became the first non-natural, man-made illicit drug of abuse. It is in the dissociative subgroup of hallucinogenic drugs and now carries a schedule II controlled substance DEA classification.

If one thinks of PCP as a parent chemical, PCP is producing a growing family of offspring drugs. Park-Davis created ketamine by making chemical modifications to PCP. Meanwhile, in clandestine laboratories, many novel PCP-derived substances have been developed. As soon as the new designer street drugs are banned, slightly modified analogues are produced to circumvent the new laws. It's a challenge for drug testing laboratories to keep up with this evolving landscape. At present, PCP is still the only member of this family in the panel of drugs included in Federal Workplace Drug Testing.

The chemical properties of PCP give it an unusually wide distribution throughout the body. Within the body, PCP can dissolve into fat, water, and alcohol. This creates a situation in which the very same dose can lead to widely different serum levels and still different intoxication levels depending on your body type, nutritional status, and alcohol use. Since the brain has a high fat content and PCP can concentrate there, the drug levels in the brain can be many times higher than the serum levels. This allows the behavioral effects to sometimes last over a week in chronic users, even though serum levels have long since plummeted. By 14 days, much of the PCP has been eliminated by the liver and excreted in urine. Since PCP can be dissolved in a person's fat cells, even after 14 days, recurrent fluctuating symptoms can occur for months if PCP is released from fat cells.

While predominantly affecting brain glutamate receptors, PCP affects many other brain receptors that can have opposing effects on a person's behavior. This gives rise to an unusual situation in which widely varying effects can occur at different doses, and the effect can change as a given dose is metabolized. It is not uncommon for intoxicated individuals to alternate between extremes of sedation and agitation.

Available data suggest that the popularity of PCP as a street drug has waxed and waned since it first emerged. From 2005 - 2011 emergency department visits related to PCP surged 4-fold. In more recent years, numbers have held steady, with the number of 12th graders

who have used PCP staying at 1% from 2016 - 2019.

There are many dangers of PCP use. Overdoses of PCP can cause seizures, brain hemorrhage from a spike in blood pressure, coma and death. PCP use can lead to tolerance, addiction, and withdrawal. The withdrawal syndrome commonly includes drug cravings, headaches, and sweating. Other issues like speech problems, memory loss, anxiety, and depression can last for a year or more after use stops. Chronic PCP users can have a symptom profile which so closely resembles schizophrenia that it may be misdiagnosed as such. In some cases, a urine drug test is ordered to distinguish between these two conditions. In fact, lab mice exposed to PCP are studied as a research model for schizophrenia. Even a single use of PCP can be dangerous because the reduced sensitivity to pain, delusions of increased physical ability, hallucinations, and agitation which can lead to serious physical injuries, both self-inflicted and accidental.

In summary, PCP is a former surgical anesthetic that has been embraced by the illicit drug industry for its easy chemistry, as well as by the scientific research community for its ability to create a schizophrenia-like syndrome in mice. PCP's fluctuating popularity, unpredictable dose to high relationship, and shifting symptom profile make it a unique drug indeed. Next month we will follow the fascinating journey of ketamine, from pharmaceutical laboratories to club drug to promising antidepressant.