CHAPTER 10

Pentachlorophenol

Pentachlorophenol (PCP) is currently registered in the United States only as a restricted use pesticide for use as a wood preservative. PCP has been used as an herbicide, algacide, defoliant, wood preservative, germicide, fungicide, and molluscicide.[1] As a wood preservative, it is commonly applied as a 0.1% solution in mineral spirits, No. 2 fuel oil, or kerosene. It is used in pressure treatment of lumber at 5% concentration. Weed killers have contained higher concentrations.

Pentachlorophenol volatilizes from treated wood and fabric. It has a significant phenolic odor, which becomes quite strong when the material is heated. Excessively treated interior surfaces may be a source of exposure sufficient to cause irritation of eyes, nose, and throat.

Technical PCP contains lower chlorinated phenols (4-12%) plus traces of chlorobenzodioxins, chlorobenzofurans, and chlorobenzenes. Incomplete combustion of PCP-treated wood may lead to the formation of these compounds.

Toxicology

PCP is readily absorbed across the skin, the lungs, and the gastrointestinal lining. In animals, the dermal LD_{50} is of the same order of magnitude as the oral. With acute exposure it is rapidly excreted, mainly in the urine, as unchanged PCP and as PCP glucuronide. In chronic exposures, the elimination half-life has been reported to be very long, up to 20 days.[2] In another study, three volunteers took consecutive oral doses of PCP, and a half-life of 20 days was also found. The long half-life was attributed to the low urinary clearance because of high protein binding.[3] In the blood, a large fraction of absorbed PCP is protein-bound. It is widely distributed to other tissues in the body, including kidney, heart, and adrenal glands.

At certain concentrations, PCP is irritating to mucous membranes and skin. Contact dermatitis is common among workers having contact with PCP. In a study of employees involved in the manufacture of PCP, chloracne was found in 7% of the workers, and the risk was significantly higher among employees with documented skin contact compared to employees without skin contact.[4] Urticaria has also been reported as an uncommon response in exposed persons.

HIGHLIGHTS

- Absorbed by skin, lung, GI lining
- Fatalities reported, associated with intensive exposure in hot environments

Signs and Symptoms:

- Irritation of the nose, throat, and eyes
- Hyperthermia, muscle spasm, tremor, labored breathing, and chest tightness indicate serious poisoning

Treatment:

- No specific antidote
- Control fever, replace fluids, oxygen
- Decontaminate eyes, skin, hair, clothing
- Monitor cardiac status, control agitation

Contraindicated:

- Salicylates for fever control

Commercial Products

Chlorophen
PCP
Penchlorol
Penta
Pentacon
Penwar
Sinituho

The sodium salt is sodium pentachlorophenate.

The primary toxicological mechanism is increased cellular oxidative metabolism resulting from the uncoupling of oxidative phosphorylation. Heat production is increased and leads to clinical hyperthermia. This clinical state may mimic the signs and symptoms found in hyperthyroidism. Internally, large doses are toxic to the liver, kidneys, and nervous system.

Based on laboratory experimentation on animals, PCP has been reported to have fetotoxic and embrotoxic properties and to bind to various hormone receptors.[5,6] Epidemiological evidence suggests exposed persons may be at risk for miscarriages, reduced birth weight, and other malformations.[7,8]

Albuminuria, glycosuria, aminoaciduria, and elevated BUN reflect renal injury. Liver enlargement, anemia, and leukopenia have been reported in some intensively exposed workers. Elevated serum alkaline phosphatase, AST, and LDH enzymes indicate significant insult to the liver, including both cellular damage and some degree of biliary obstruction.

Signs and Symptoms of Poisoning

The most common effects of airborne PCP include local irritation of the nose, throat, and eyes, producing a stuffy nose, scratchy throat, and tearing. Dermal exposure is also common and may lead to irritation, contact dermatitis, or more rarely, diffuse urticaria or chloracne. Individual cases of exfoliative dermatitis of the hands and diffuse urticaria and angioedema of the hands have been reported in intensively exposed workers. Several infant deaths occurred in a nursery where a PCP-containing diaper rinse had been used.

Severe poisoning and death have occurred as a result of intensive PCP exposure. Acute poisoning occurs with systemic absorption which can occur by any route of sufficient dosage. Most occupational poisonings occur through dermal contact. Hyperthermia, muscle spasm, tremor, labored breathing, and chest tightness indicate serious poisoning. The patient may also complain of abdominal pain, and exhibit vomiting, restlessness, and mental confusion. Tachycardia and increased respiratory rate are usually apparent. Other commonly reported signs and symptoms of systemic poisoning include profuse sweating, weakness, dizziness, anorexia, and intense thirst. Workers exposed over long periods may experience weight loss.

Most adult fatalities have occurred in persons working in hot environments where hyperthermia is poorly tolerated. Cases of aplastic anemia and leukemia have been reported which were associated temporally with PCP exposure. Causal relationships in these cases were not established.[9] Peripheral neuropathies have also been reported in some cases of long-term occupational exposure; however, a causal relationship has not been supported by longitudinal studies.[10]

Confirmation of Poisoning

If poisoning is strongly suspected on the basis of exposure, symptoms, and signs, **do not postpone treatment** until diagnosis is confirmed.

PCP can be measured in blood, urine, and adipose tissue by gas-liquid chromatography. Plasma levels can be much greater than urine levels (ratio of blood to urine is 1.0 to 2.5) so care must be taken in interpreting results.[10,11] There is no clear-cut determination of what constitutes an abnormally high level of PCP, and there is great variability among different references. Most information on the extent of serum levels in relation to toxicity is based on individual cases or small series of patients. Reports exist of asymptomatic infants with serum levels as high as 26 parts per million (ppm).[11,12] However, most reports of non-occupational exposure in the general public involve levels in the parts per billion range.[1,13-15] Food is probably the main source of this nanogram-level dosage.[1] Serum levels among occupationally exposed persons often exceed 1 ppm.[1] A report of a lethal case describes a plasma level of 16 ppm,[16] but most cases generally involve serum levels in the range of 100 ppm or higher.[11,17] It is reasonable to assume that levels greater than 1 ppm are consistent with an unusual exposure and that levels approaching 100 ppm are cause for great concern.

Treatment

1. Supportive treatment and hyperthermia control. There is no specific antidote to the poisoning; therefore treatment is supportive in nature including oxygen, fluid replacement, and most importantly, fever control.

Reduce elevated body temperature by physical means. Administer sponge baths and use fans to increase evaporation.[18] In fully conscious patients, administer cold, sugar-containing liquids by mouth as tolerated. Cooling blankets and ice packs to body surfaces may also be used.

Antipyretic therapy with salicylates is **strongly contraindicated** as salicylates also uncouple oxidative phosphorylation. Other antipyretics are thought to be of no use because of the peripherally mediated mechanism of hyperthermia in poisoning of this nature. Neither the safety nor the effectiveness of the other antipyretics has been tested.

Administer oxygen continuously by mask to minimize tissue anoxia. Unless there are manifestations of cerebral or pulmonary edema or of inadequate renal function, administer intravenous fluids to restore hydration and support physiologic mechanisms for heat loss and toxicant disposition. Monitor serum electrolytes, adjusting IV infusions to stabilize electrolyte concentrations. Follow urine contents of albumin and cells, and keep an accurate hourly record of intake/output to forestall fluid overload if renal function declines.

Caution: In the presence of cerebral edema and/or impaired renal function, intravenous fluids must be administered very cautiously to avoid increased

intracranial pressure and pulmonary edema. Central monitoring of venous and pulmonary wedge pressures may be indicated. Such critically ill patients should be treated in an intensive care unit.

2. Skin decontamination. Flush the chemical from eyes with copious amounts of clean water. Perform skin decontamination as described in Chapter 2.

3. Cardiopulmonary monitoring. In severe poisonings, monitor pulmonary status carefully to insure adequate gas exchange, and monitor cardiac status by ECG to detect arrhythmias. The toxicant itself and severe electrolyte disturbances may predispose to arrhythmias and myocardial weakness.

4. Neurological. To reduce production of heat in the body, control agitation and involuntary motor activity with sedation. Lorazepam or other benzodiazepines should be effective, although use of these drugs in these poisonings has not been reported. If lorazepam is chosen, administer slowly, intravenously.

Dosage of Lorazepam:

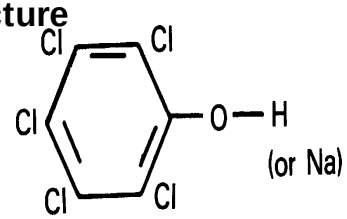
- *Adults:* 2-4 mg/dose IV given over 2-5 minutes. Repeat if necessary to a maximum of 8 mg in a 12-hour period.
- *Adolescents:* Same as adult dose, except maximum dose is 4 mg.
- *Children under 12 years:* 0.05-0.10 mg/kg IV over 2-5 minutes. Repeat if necessary 0.05 mg/kg 10-15 minutes after first dose, with a maximum dose of 4 mg.

Caution: Be prepared to assist pulmonary ventilation mechanically if respiration is depressed, to intubate the trachea if laryngospasm occurs, and to counteract hypotensive reactions.

5. Gastrointestinal decontamination. If PCP has been ingested in a quantity sufficient to cause poisoning and the patient presents within one hour, consider gastric decontamination as outlined in Chapter 2.

6. Nutrition. During convalescence, administer a high-calorie, high-vitamin diet to restore body fat and carbohydrates. Discourage subsequent contact with the toxicant for 4-8 weeks (depending on severity of poisoning) to allow full restoration of normal metabolic processes.

Chemical Structure



References

1. Jorens PG and Schepens PJC. Human pentachlorophenol poisoning. *Hum Exp Toxicol* 1993;479-95.
2. Kalman DA and Horstman SW. Persistence of tetrachlorophenol and pentachlorophenol in exposed woodworkers. *J Toxicol Clin Toxicol* 1983;20:343.
3. Uhl S, Schmid P, and Schlatter C. Pharmacokinetics of pentachlorophenol in man. *Arch Toxicol* 1986;58:182-6.
4. O'Malley MA, Carpenter AV, Sweeney MH, et al. Chloracne associated with employment in the production of pentachlorophenol. *Am J Ind Med* 1990;17:411-21.
5. Danzo BJ. Environmental xenobiotics may disrupt normal endocrine function by interfering with the binding of physiological ligands to steroid receptors and binding proteins. *Environ Health Perspect* 1997;105:294-301.
6. Tran DQ, Klotz DM, Ladlie BL, et al. Inhibition of progesterone receptor activity in yeast by synthetic chemicals. *Biochem Biophys Res Commun* 1996;229:518-23.
7. Dimich-Ward H, Hertzman C, Teschke K, et al. Reproductive effects of paternal exposure to chlorophenate wood preservatives in the sawmill industry. *Scand J Work Environ Health* 1996;22:267-73.
8. DeMaeyer J, Schepens PJ, Jorens PG, and Verstaete R. Exposure to pentachlorophenol as a possible cause of miscarriages. *Br J Obstet Gynaecol* 1995;102:1010-1.
9. Roberts HJ. Aplastic anemia due to pentachlorophenol. *New Engl J Med* 1981;305:1650-1.
10. Casarett LJ, Bevenue A, Yauger WL, and Whalen SA. Observations on pentachlorophenol in human blood and urine. *Am Ind Hyg Assoc J* 1969;30:360-6.
11. Clayton GD and Clayton FE (eds). Patty's Industrial Hygiene and Toxicology, vol 2B, 4th ed. New York: John Wiley & Sons, 1994, pp. 1605-13.
12. Robson AM, Kissane JM, Elvick WH, et al. Pentachclorophenol poisoning in a nursery for newborn infants: Clinical features and treatment. *J Pediatr* 1969;75:309-16.
13. Gomez-Catalan J, To-Figueras J, Planas J, et al. Pentachlorophenol and hexachlorobenzene in serum and urine of the population of Barcelona. *Hum Toxicol* 1987;6:397-400.
14. Wylie JA, Gabica J, Benson WW, and Yoder J. Exposure and contamination of the air and employees of a pentachlorophenol plant, Idaho-1972. *Pest Monit J* 1975;9:150-3.
15. Wagner SL. Pentachlorophenol. In: Clinical Toxicology of Agricultural Chemicals. Corvallis, OR: Oregon State University Press, 1981, pp. 131-7.
16. Wood S, Rom WN, White GL, and Logan DC. Pentachlorophenol poisoning. *J Occup Med* 1983;25:527-30.
17. Gray RE, Gilliland RD, Smith EE, et al. Pentachlorophenol intoxication: Report of a fatal case, with comments on the clinical course and pathologic anatomy. *Arch Environ Health* 1985;40:161-4.
18. Graham BS, Lichtenstein MJ, Hinson JM, et al. Nonexertional heatstroke: Physiologic management and cooling in 14 patients. *Arch Intern Med* 1986;146:87-90.