ATSDR

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Case Studies in Environmental Medicine

23 Pentachlorophenol Toxicity

Environmental ALERT . . .

- ***Pentachlorophenol was one of the most widely used biocides in the United States. Although it is no longer available to the general public, it continues to be an exposure risk.***
- ***Exposures can occur from volatilization of the chemical from treated surfaces and from skin contact with treated wood.***
- ***Pentachlorophenol has been found at about 235 of the more than 1,300 hazardous waste sites on the National Priorities List.***

This monograph is one in a series of self-instructional publications designed to increase the primary care provider's knowledge of hazardous substances in the environment and to aid in the evaluation of potentially exposed patients. See page 16 for more information about continuing medical education credits and continuing education units.

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U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Agency for Toxic Substances and Disease Registry

ATSDR

How to use this issue...

This issue begins with a composite case study that describes a realistic encounter with a patient. This description is followed by a pretest. The case study is further developed through Challenge questions at the end of each section. To fully benefit from this monograph, readers are urged to answer each question when it is presented. (Answers to the Pretest and Challenge questions are found on pages 14-15.) The monograph ends with a posttest, which can be submitted to the Agency for Toxic Substances and Disease Registry (ATSDR) for continuing medical education (CME) credit or continuing education units (CEU). See page 16 for further instructions on how to receive these credits.

The objectives of this monograph on pentachlorophenol are to help you

- ❑ **Explain why pentachlorophenol may be an acute and chronic health hazard**
- ❑ **Describe the factors that may contribute to pentachlorophenol poisoning**
- ❑ **Identify potential environmental and occupational sources of pentachlorophenol exposure**
- ❑ **Identify evaluation and treatment protocols for pentachlorophenol exposure**
- ❑ **List sources of information on pentachlorophenol**

Contents

This issue is prepared with the assistance of those who share a common concern for physician education, public health, and the environment, including the following organizations: American Academy of Clinical Toxicology, American Academy of Family Physicians, American Academy of Pediatrics, American College of Emergency Physicians, American College of Occupational and Environmental Medicine, American Medical Association, Association of State and Territorial Health Officials, and the Society of Teachers of Family Medicine. Final responsibility for the contents and views expressed in this monograph resides with ATSDR.

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Case Study

A 63-year-old male with weight loss, fever, dyspnea, and rash

On a hot, humid summer day, a 66-year-old male with complaints of anorexia, weight loss, flu-like symptoms, shortness of breath, and rash is brought to your office by his son. His fever, which began last evening, has been recurring since shortly after he moved to this locale to be near his son and grandchildren about 10 months ago. While the patient is at his son's home, in the company of his grandchildren, he seems to improve; yet when the patient returns to his home, he becomes ill. The son mentions that his father generally has been withdrawn and housebound since he broke his hip a year ago. The patient lives in a log cabin that has only natural ventilation and is heated by a wood stove.

Physical examination reveals a well-nourished male, sweating profusely and mildly tachypneic. He exhibits confusion and is oriented to person only. His blood pressure is 132/70 sitting, pulse 120/minute and regular, respiratory rate 24/minute and shallow without stridor. He has a rectal temperature 104.7°F. He has no cough and no vomiting or diarrhea. The skin is warm and moist; the mucous membranes are wet. There is a papular erythematous rash on the forearms bilaterally and on the neck. There is no skin discoloration, acne, or conjunctivitis. There are no focal neurologic findings, including no Kernig's or Brudzinski's signs. The lungs are clear to auscultation and percussion. There is no costovertebral tenderness. Bowel sounds are normal, and the remainder of the abdominal examination is unremarkable. You admit the patient to the hospital.

Further history reveals that the patient is a retired botanist. He had been active and generally well before the fall in which he fractured his hip. He is being treated for mild hypertension with a diuretic. There is no other significant medical or surgical history. For the past 6 months, the patient has been taking amitriptyline for depression as prescribed by his former personal physician, and he has been treating his flu-like symptoms with aspirin at the recommended over-the-counter doses. He is using calamine lotion daily on the rash. He admits to being generally withdrawn and home-bound but denies any thoughts of suicide.

Initial laboratory values show a serum pH of 7.39, $Paco_2$ 21 and Pao_2 120 on 2 liters of oxygen. Serum electrolytes reveal the following: sodium 131 mEq/L (normal 135–148); potassium 5.1 mEq/L (normal 3.5–5.3); chloride 83 mEq/L (normal 95–105); and bicarbonate 21 mEq/L (normal 22–28). The anion gap is 32. Blood urea nitrogen is 32 mg/dL (normal 5–20) and creatinine 2.8 mg/dL (normal 0.7–1.5). The urinalysis is normal; urine pH is 5.5. Initial white blood count is 11.7 x $10^3/mm^3$ (normal 4.5–11 x 10^3) with 61% neutrophils (normal 60%); the spun hematocrit is 47% (normal 42%–52%). Blood salicylate level of 5 mg/dL is within the therapeutic range.

(a) What would you include in this patient's problem list?

(b) What is the differential diagnosis for this patient?

(c) Is the patient's condition due to depression? heat stroke?

(d) What further information will you seek to make a diagnosis?

Answers to the Pretest questions are on page 14.

Exposure Pathways

Pentachlorophenol (C_6Cl_5OH) and its sodium salt (sodium pentachlorophenate) are used as preservatives in the manufacture and treatment of a variety of commercial products to prevent decay from microorganisms such as fungi, mold, algae, and mosses. Treated products include particleboard, textiles, paints, adhesives, leather, latex, rubber, pulp, paper, starches, and wood. Pentachlorophenol has also been used extensively around the home as an herbicide, fungicide, weed and brush killer, disinfectant, and wood-preserving compound. Worldwide production estimates range as high as 90 million pounds; 80% of U.S. consumption is as a wood preservative, primarily for telephone and power-line poles.

- **In 1987, EPA banned pentachlorophenol for all nonwood products.**

A common acronym for pentachlorophenol is PCP, which is used throughout this document. The street drug phencyclidine (angel dust) is also referred to as PCP but has a different pathophysiology and has no chemical relationship to pentachlorophenol.

PCP was one of the most widely used biocides in the United States. Because of its suspected carcinogenicity, however, in 1987, the Environmental Protection Agency (EPA) banned all uses of PCP except those for wood products and restricted its availability and use to certified applicators. PCP is no longer available to the general public, which accounted for only about 3% of the amount used.

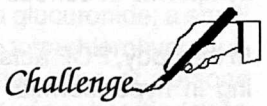
- **Even "untreated" lumber typically is sprayed with or dipped in pentachlorophenol before it leaves the mill.**

Most lumber produced commercially in the United States is still treated routinely with sodium pentachlorophenate solution. To control fungal growth and sap stain, a typical sawmill will apply a solution of the sodium salt to the lumber in a spray box immediately before grading and stacking. Pressure-treating wood to thoroughly impregnate it with PCP results in "penta" wood, a product commonly used to build outdoor structures such as residential fences, decks, and equipment for children's playgrounds. Penta wood is desirable because it retains its natural appearance, emanates little odor, and accepts paint easily.

Logs for use in the ground typically are treated with PCP and arsenical salts as preservatives against microorganisms and termites, then coated with creosote, a distillate of coal tar, to form a barrier to moisture and to prevent leaching of the PCP and arsenical salts. PCP has traditionally been used in log homes. Volatilization from the surface of PCP-treated products is estimated at an annual rate of roughly 2% of the total amount applied. In log homes, this volatilization rate has resulted in indoor-air contamination high enough to cause PCP-related symptoms in inhabitants.

Due to the extensive use of PCP throughout the United States, it is present in air, water, and soil. Contaminated food and water supplies are common sources of human intake, although the amounts in-

gested typically are small. PCP gets into water through wastewater discharges from leather tanning and textile factories, municipal wastewater treatment facilities, pulp and paper mills, and wood treatment plants. Soil contamination occurs as a result of runoff from PCP's past use as an herbicide, leaching from treated wood products and spills at industrial facilities and hazardous waste sites. PCP is a stable compound, but in water it undergoes photooxidation by sunlight (half-life 3 to 100 hours depending on pH) and can be biotransformed by microorganisms in the soil (half-life 2 to 4 weeks). One of the degradation products of PCP is tetrachlorophenol, which is also toxic.



Additional information for the case study: For years, the patient's hobbies have included woodworking, small-boat building, and organic gardening. Because of his ill health, however, he has not done any of these activities for the past several months. He spends most of his time indoors. The patient comments that his dog is his only interest now, and the dog seems to get sick when he does.

(1) What are some clues in this case that might lead you to suspect a possible toxic environmental exposure?

Who's at Risk

The greatest risk of exposure to PCP occurs from occupational manufacture and use of the compound, especially in poorly ventilated areas. Pest-control applicators who used PCP in indoor settings were at great risk from inhalation exposures. Dermal exposure occurs primarily to those in trades or professions that handle wood, such as carpenters, electric utility-line workers, lumber-mill workers, and dock loaders. Sawmill workers are at potential risk due to inhalation of contaminated wood dust and volatilized PCP when penta wood is cut, especially freshly treated wood.

- **Infants and children are predisposed to increased PCP exposure by their greater surface area-to-weight ratios, as well as hand-to-mouth and play behaviors.**

- **Living in log homes or other structures where PCP has been used as a preservative increases risk to inhabitants.**

PCP continues to leach out of pressure-treated wood for many years. Log homes and older dwelling structures where PCP has been used as a preservative have been found to have PCP levels in indoor air exceeding those set for the workplace. Chronic exposure of occupants of log cabins and older homes has resulted in PCP toxicity.

There is some evidence that children are more susceptible to the toxic effects of PCP than adults, and that infants are even more susceptible than children, especially by the dermal route of exposure. In addition, infants and children may be at increased risk because of greater body surface area-to-body weight ratios, higher respiratory rates, hand-to-mouth behaviors, and play habits. Neonates exposed to PCP in contaminated diapers and bed linens exhibited signs and symptoms of serious poisoning.

- **Medications and environmental conditions that predispose a person to hyperthermia increase the risk of adverse effects to PCP-exposed persons.**

In the body, PCP acts to uncouple oxidative phosphorylation, resulting in hyperthermia. PCP-exposed workers in environments that prevent dissipation of heat from the body (e.g., high temperatures and high humidity) may be more susceptible to its acute toxic effects. Medications that cause dehydration or possess anticholinergic properties may also increase the susceptibility of exposed persons to hyperthermia. Aspirin, which can also uncouple oxidative phosphorylation when absorbed in large amounts, may enhance the risk of toxicity for PCP-exposed persons. Because PCP is highly protein-bound, persons taking medications on a long-term basis that have a high affinity for plasma proteins may be at increased risk of PCP-induced toxicity. Phenytoin, the anticoagulant warfarin, diuretics such as furosemide and ethacrynic acid, and anti-inflammatory agents such as ibuprofen and naproxen can compete with PCP for protein-binding sites, thereby increasing the level of free PCP that is circulating in the blood.

Challenge

(2) What factors could place the patient in the case study at increased risk for pentachlorophenol poisoning?

Biologic Fate

Pulmonary absorption of vapors, aerosols, and dusts are significant routes of exposure to PCP. PCP and its sodium salt are also absorbed readily via the skin and the gastrointestinal tract.

- **PCP is absorbed readily via the skin, respiratory tract, and gastrointestinal tract.**

Data on distribution of PCP in the body are limited; however, PCP is lipophilic, which presumably plays a role in determining its distribution. In autopsy studies, PCP was detected in the liver, kidneys, and brain, with smaller amounts in spleen and adipose tissue.

PCP is highly protein-bound in the blood and is not readily metabolized. In the liver, most PCP is conjugated to a glucuronide; a small amount undergoes oxidative dechlorination to tetrachlorohydroquinone (TCH), which has been detected in the urine of persons occupationally exposed. Ultimately, about 86% of an absorbed dose is excreted in the urine. Biliary excretion occurs in humans, but with extensive enterohepatic recirculation, only a small amount of pentachlorophenol (about 4% of an administered oral dose) is detected in the feces. Pentachlorophenol is also excreted in the milk of lactating humans and animals.

The results of studies conducted in workers suggest that the PCP excretion rate differs between acute high-level exposure and chronic low-level exposure. Elimination half-lives of about 10 hours were found in volunteers undergoing an acute (45-minute) controlled inhalation exposure, whereas the elimination half-life in chronically exposed workers on vacation was 19 to 20 days. The slower elimination of PCP in chronically exposed workers may be a result of an established equilibrium between lung, plasma protein, urine, and tissue deposits.

- **PCP is excreted largely unchanged in the urine; a small amount is metabolized in the liver.**

Physiologic Effects

It is believed that PCP's high degree of binding to proteins may induce conformational changes in enzymes involved in oxidative phosphorylation. Oxidative phosphorylation is the process whereby electrons generated from various sources such as the tricarboxylic acid cycle are transported down the cytochrome system. This transport normally results in the consumption of O_2 (cellular respiration) and the production of a substantial amount of energy that is captured in the production of high-energy phosphate bonds (i.e., adenosine triphosphate [ATP] bonds). The energy in these bonds is later used during other biochemical reactions.

- **The acute toxicity of PCP is due primarily to its ability to uncouple mitochondrial oxidative phosphorylation.**

When the formation of high-energy phosphate bonds is blocked by PCP but electron transport continues, then the process of oxidative phosphorylation is said to be uncoupled. Uncoupling results in cellular energy being released as heat, which produces hyperpyrexia. PCP also causes active transport pumps within cell membranes to fail, resulting in electrolyte gradient loss, fluid shifts, and eventual cell death.

In humans, many of the effects of acute PCP exposure are probably secondary to hyperthermia, including neurologic effects and rhabdomyolysis. In addition, metabolic acidosis can develop from accelerated aerobic metabolism.

- **PCP toxicity manifests primarily as a clinical syndrome of hyperthermia with associated rhabdomyolysis.**

Generally, humans are exposed to technical-grade PCP, which may be contaminated with dibenzodioxins, dibenzofurans, diphenyl ethers, chlorophenoxyphenols, and other chlorinated congeners—all of which are suspected to be carcinogenic or known to produce other adverse effects. Animal studies with both technical and purified PCP have demonstrated that many, but not all, of the toxic effects attributed to PCP are actually due to impurities.

Neurologic Effects

- **Neurologic effects from PCP exposure are most likely the direct result of hyperthermia.**

Human case reports of PCP exposure suggest that there are central and peripheral nervous system effects of toxicity. The neurologic effects that manifest after PCP exposure are most likely the result of hyperthermia and not a direct effect of PCP on the nervous system. Persons acutely exposed to PCP may experience lethargy, tachypnea, tachycardia, intermittent delirium, seizures, cerebral edema, focal swelling of the myelin sheath, and respiratory distress. Signs indicative of central nervous system toxicity in a 3-year-old girl exposed to PCP via the domestic water supply included intermittent delirium, fever, and convulsions. No adverse effects on the central or peripheral nervous systems have been reported after chronic occupational exposure to PCP.

Hepatic Effects

- **There is ample evidence of hepatotoxicity in experimental animals exposed to purified PCP.**

Hepatic toxicity in humans, as manifested by elevated serum SGOT (AST) and SGPT (ALT) levels, hepatomegaly, fatty infiltration of the liver and centrilobular congestion and degeneration, was seen after fatal and nonfatal acute exposures to PCP. However, contaminants of technical-grade PCP or exposure to other chemicals may be responsible for some of this damage. In experimental animal studies that compared the hepatic toxicity of equal doses of technical and purified PCP, the effects associated with the purified preparation were less severe than those seen with the technical grades in most cases. Some ultrastructural changes observed in the mitochondria of liver cells of the animals treated with technical-grade PCP were consistent with uncoupling of oxidative phosphorylation.

Renal Effects

In humans and animals, PCP exerts a minor toxic effect on the kidneys, producing only mild and transient disturbances. Workers at a wood-treatment facility had reduced glomerular filtration rates and mild tubular degeneration, which were reversible when exposure ceased. Other evidence of renal dysfunction in humans, such as impaired acid-base balance, may be secondary to hyperthermia. In animals, little or no consistent difference was seen between technical-grade and purified PCP with regard to severity of renal effects.

❑ **Renal effects from PCP exposure are mild and transient.**

Carcinogenicity

There is no convincing evidence from epidemiologic studies that PCP causes cancer in humans. Case reports suggest a possible association between cancer (Hodgkin's disease, soft-tissue sarcoma, and acute leukemia) and occupational exposure to technical-grade PCP. However, in all of these cases, concurrent exposure to other toxic substances may have contributed to the effects. In a study by the National Toxicology Program (NTP), pure PCP showed oncogenic activity in mice. The International Agency for Research on Cancer (IARC) considers the evidence for carcinogenicity of PCP in humans limited, and the evidence for carcinogenicity in animals inadequate. The EPA carcinogenic classification for PCP is "probable human carcinogen," but this classification is currently under review.

❑ **Case reports suggest that an association exists between technical-grade PCP and Hodgkin's disease and soft-tissue sarcoma.**

Other Effects

Chronic exposure to technical-grade PCP has been associated with chloracne—an acneiform rash around the eyes, temples, and forehead. This skin condition, as well as many other effects of PCP, has been attributed to various contaminants in technical-grade PCP, particularly dioxins and dibenzofurans. Pemphigus vulgaris and urticaria (skin diseases with an immunologic pathophysiology) have been reported in several cases of nonoccupational exposures. Depigmentation (or vitiligo) and irritant dermatitis have been associated with chronic exposure to PCP-containing germicides. Low-level chronic exposures to airborne PCP can cause irritation of the eyes, nose, throat, and lungs.

Case reports have been published of hemolytic anemia and aplastic anemia with subsequent acute leukemia or Hodgkin's disease. The exposures were predominantly dermal exposures to technical-grade PCP. The mechanism for these hematologic effects appears to be a direct action on blood-forming tissue. The reported anemia is unlikely to be caused by uncoupling of oxidative phosphorylation because no signs of hyperthermia were observed in these cases.

❑ **Other reported effects of PCP exposure include skin lesions and hematologic abnormalities. Most of these effects may be due to the impurities in technical-grade PCP.**

Animals exposed to technical-grade PCP exhibited hematologic effects that generally were not observed when the animals were administered pure PCP.

There is no evidence that PCP exposure results in human embryotoxicity or teratogenicity. In experimental animals, PCP is not teratogenic but is embryotoxic and fetotoxic at exposure levels that cause maternal toxicity.

Additional information for the case study: Suspecting an environmental toxic exposure, you contact an environmental toxicologist at the state health department. After discussing the patient and his symptoms, the specialist suggests poisoning caused by an organophosphate pesticide, dinitrophenol, or pentachlorophenol.

(3) What is the reasoning that leads you to narrow the diagnosis to pentachlorophenol poisoning?

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_____

Clinical Evaluation

History and Physical Examination

- **A thorough environmental and occupational history may reveal a possible PCP exposure in cases in which hyperthermia occurs.**

The history of a person who has possible PCP exposure should include information about other precipitating factors for hyperthermia such as age; clothing; environmental temperature and humidity; medications with anticholinergic effects, such as phenothiazines, antihistamines, and antidepressants; medications that predispose to dehydration, such as diuretics; medications or chemicals that uncouple oxidative phosphorylation, such as salicylates or dinitrophenols; and medications that interfere competitively with protein binding, such as warfarin, phenytoin, furosemide, and ibuprofen. A thorough environmental and occupational history should be obtained, including information about hobbies or projects such as woodworking and gardening. (See *Case Studies in Environmental Medicine:Taking an Exposure History.*)

Because PCP-intoxicated patients may not give the appearance of having an elevated temperature, the physical examination must include a core body temperature. In addition, blood pressure and heart and respiratory rate should be determined. The liver, kidney,

and central nervous system may be affected by PCP exposure. Because exposure to technical-grade PCP has been associated with chloracne and other skin conditions, respiratory irritation, and blood dyscrasias, the skin, respiratory tract, and blood should be evaluated.

Signs and Symptoms

Acute Exposure

Acute exposure to PCP is associated with hyperthermia, which produces a generalized spectrum of toxicity, including anorexia, fatigue, thirst, fever, profuse diaphoresis, tachypnea, tachycardia, nausea, vomiting, and abdominal pain. In severe poisonings, severe muscle spasms and rigidity, as well as seizures, may occur. Hepatic enlargement has been reported in adults and infants exposed to PCP-containing compounds. Hepatic toxicity has been further manifested in adults by increased SGOT (AST) and SGPT (ALT), fatty degeneration, and congestion. Intravascular hemolysis and aplastic anemia have been associated with PCP exposure in case reports. There is no significant staining of the skin after dermal contact with PCP as there is with dinitrophenols, which also cause uncoupling of oxidative phosphorylation.

❑ **Most signs and symptoms of acute PCP poisoning are the result of hyperthermia.**

Chronic Exposure

In addition to nonspecific signs and symptoms, such as fever and malaise, chronic occupational exposure to high levels of PCP vapor, as well as to aerosols, has been associated with conjunctivitis, chronic sinusitis, bronchitis, and reduced glomerular filtration and tubular function. There is evidence of elevated SGOT and SGPT levels in workers after chronic, predominantly dermal, exposure to PCP. Most of these conditions are reversible after exposure ceases. One group of workers with chronic PCP exposure had a high incidence of chloracne, most likely due to PCP contaminants.

❑ **Nonspecific signs and symptoms such as fever, anorexia, weight loss, and fatigue characterize chronic PCP exposure.**

Laboratory Tests

Direct Biologic Indicators

In one study, the general population had average levels of 4 micrograms of PCP per deciliter (µg/dL) of blood and 5 micrograms of PCP per liter (µg/L) of urine. In studies of workers using PCP or PCP-treated materials (e.g., workers involved in construction of log homes, repair of telephone lines, custodial care of log cabin museums, application of pesticides) PCP blood levels ranged from 8.3 to 5,760 µg/dL and urinary levels ranged from 120 to 10,000 µg/L.

❑ **PCP can be measured in urine and blood.**

Residents of log homes treated with PCP preservatives had mean levels of 42 µg/dL in blood and 69 µg/L in urine; PCP blood levels of children who resided in log homes were 1.8 times the blood levels of their parents.

When monitoring urine levels, relating the PCP concentration to the amount of creatinine in the sample (i.e., µg PCP per gram of creatinine [µg/g creatinine]) corrects for variations in urine concentration. The American Conference of Governmental Industrial Hygienists (ACGIH) suggests that the biological exposure index (BEI) guideline for PCP in the workplace be 1,000 µg/g creatinine.

Indirect Biologic Indicators

In PCP poisoning, laboratory evaluation should include tests for hepatic and renal dysfunction, electrolyte imbalance, hemolytic anemia, and metabolic acidosis. Testing of immune function is not warranted in the clinical management of PCP exposure.

Challenge

Additional information for the case study: You tell the patient and his son that the patient's symptoms are consistent with pentachlorophenol exposure and the source may be the logs of the cabin.

(4) What tests can help you confirm your suspicion?

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_____

(5) What further laboratory evaluation is appropriate for the patient, assuming his condition is due to pentachlorophenol exposure?

_____

_____

(6) The son asks you if his father's exposure to pentachlorophenol is increased by using throat lozenges; the label says the lozenges contain 50 milligrams of phenol per lozenge. What will you tell him?

_____

_____

Treatment and Management

Acute Exposure

The treatment of pentachlorophenol poisoning is supportive. The onset of toxicity may be sudden in persons with significant exposure. Thus, it will be necessary to stabilize the patient with maintenance of the airway, breathing, and circulation. Patients who have seizures will require pharmacotherapy with benzodiazepines. If intubation is necessary, general anesthesia or paralysis may be required to reduce injury or prevent death during the procedure. Gastric lavage will be useful only if the patient has recently ingested the substance. Activated charcoal has been shown to bind most phenolic compounds; repeated dosing may be useful in preventing absorption and in interrupting enterohepatic recirculation. Cholestyramine resin was also used for this purpose in primates, but its effectiveness in humans is unknown. Forced diuresis has been proposed as enhancing the elimination of PCP; however, the clinical evidence to justify this therapy is lacking and volume depletion in patients with hyperthermia should be avoided.

After removal from exposure and decontamination, cooling the patient is of the utmost importance in the treatment of hyperthermia. The patient's temperature can be reduced with an ice-water bath or repeated washes with cool water in front of fans.

Chronic Exposure

Treatment of chronic pentachlorophenol poisoning involves removal from the source of exposure.

(7) What treatment would you recommend for the patient in the case study? What follow-up measures would you recommend for managing this case?

Standards and Regulations

Workplace

The Occupational Safety and Health Administration (OSHA) has set a permissible exposure limit (PEL) for PCP of 0.5 milligrams per cubic meter (mg/m^3) of air as an 8-hour time-weighted average (TWA). OSHA also gives PCP a "skin" designation, which indicates the potential for dermal absorption. The National Institute for Occupational Safety and Health (NIOSH) has determined the level immediately dangerous to life and health (IDLH) to be 150 mg/m^3 in air.

Environment

In 1984, EPA restricted the use of PCP to wood products. In addition, EPA set restrictions on the dioxin levels allowed in pentachlorophenol products.

The EPA maximum contaminant level (MCL) for PCP in drinking water is 1 µg/L (1 part per billion [ppb]); the EPA maximum contaminant level goal (MCLG) is 0 µg/L. Several states have guidelines for drinking water ranging from 6 to 220 µg/L. The World Health Organization (WHO) guideline for PCP in drinking water is 10 µg/L (10 ppb).

The Food and Drug Administration (FDA) lists PCP as safe for use as a component of adhesives intended for use in packaging, transporting, or holding food.

Suggested Reading List

Clinical

Wood S, Rom WN, White GL, Logan DC. Pentachlorophenol poisoning. J Occup Med 1983;25(7):527-30.

Exon JH. A review of chlorinated phenols. Vet Hum Toxicol 1984;26(6):508-20.

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.

Epidemiology

Gilbert FI, Minn CE, Duncan RC, Wilkinson J. Effects of pentachlorophenol and other chemical preservatives on the health of wood treating workers in Hawaii. Arch Environ Contam Toxicol 1990;19:603-9.

Enarson DA, Chan-Yeung M, Embree V, et al. Occupational exposure to chlorophenates. Scand J Work Environ Health 1986;12:144-8.

Thind KS, Karmali S, House RA. Occupational exposure of electrical utility linemen to pentachlorophenol. Am Ind Hyg Assoc J 1991;52(12):547-52.

Cline RE, Hill RH Jr, Phillips DL, et al. Pentachlorophenol measurements in body fluids of people in log homes and workplaces. Arch Environ Contam Toxicol 1989;18:475-81.

Toxicology

Williams PL. Pentachlorophenol, an assessment of the occupational hazard. Am Ind Hyg Assoc J 1982;43(11):799-810.

Seiler JP. Pentachlorophenol. Mutat Res 1991;257:27-47.

Related Government Documents

Agency for Toxic Substances and Disease Registry. Toxicological profile for pentachlorophenol [update]. Atlanta: US Department of Health and Human Services, Public Health Service, 1993.

Environmental Protection Agency. Drinking water criteria document for pentachlorophenol. Washington, DC: US Environmental Protection Agency, Office of Drinking Water, 1989. Report no. EPA 600/x 84-177-1.

Sources of Information

More information on the adverse effects of pentachlorophenol and treating cases of exposure can be obtained from ATSDR, your state and local health departments, and university medical centers. *Case Studies in Environmental Medicine: Pentachlorophenol Toxicity* is one of a series. To obtain other publications in this series, please use the order form on the inside back cover. For clinical inquiries, contact ATSDR, Division of Health Education, Office of the Director, at (404) 639-6204.

Answers to Pretest and Challenge Questions

Pretest

Pretest questions begin on page 1.

(a) The patient's problem list is as follows:

- Fever of undetermined cause (hyperthermia)
- Mildly altered mental status
- History of depression, currently under treatment
- History of hypertension, currently under treatment
- Electrolyte abnormalities
- Azotemia
- Erythematous rash

(b) The differential diagnosis for a patient who has high fever, tachypnea, and mildly altered mental status must include acute overwhelming infections such as pneumonia, meningitis, or urinary tract infection. In addition, the patient might be suffering from heat stroke and heat exhaustion (see [c] below), or he may be suffering from hyperthermia due to medications or chemical exposure. Heat-related disorders are exacerbated by dehydration and diuretic use.

(c) No; depression would not cause fever, electrolyte abnormalities, azotemia, or rash. However, the medications he is taking for depression may be contributing factors. Heat stroke is unlikely because this condition is usually characterized by relatively dry skin and dry mucous membranes, and this patient is suffering from diaphoresis.

(d) Before making a diagnosis, you should explore the conditions in the differential diagnosis. Infection should be ruled out early in the management of this case; you may need to perform a lumbar puncture and obtain blood and urine cultures. A chest X ray, urinalysis, intravenous pyelogram, and liver function tests may provide information to help exclude conditions in the differential diagnosis. Resources to explore chemical poisonings can be found at your local or state health department, ATSDR, and the regional poison control center.

Challenge

Challenge questions begin on page 3.

(1) Some clues that indicate a possible environmental exposure, particularly in the home, include the following: (1) a temporal relationship between the patient's onset of symptoms and presence in the home, and (2) the simultaneous illness of the patient and his dog. It is not uncommon for illnesses in pets to suggest toxic environmental exposures. (See *Case Studies in Environmental Medicine: Taking an Exposure History.*)

(2) Any factors that contribute to hyperthermia could increase the risk for PCP poisoning. Factors for the patient in the case study include the following: the age of the patient; environmental conditions (the heat and humidity) that prevent heat dissipation; the use of a diuretic (which could enhance dehydration and increase the amount of circulating PCP by competing with it for protein-binding sites); the use of a tricyclic antidepressant (which has anticholinergic effects); and the use of aspirin (which causes further uncoupling of oxidative phosphorylation if taken in excessive amounts).

(3) Organophosphate pesticides, whose mechanism of action is based on acetylcholinesterase inhibition, may cause a syndrome of cholinergic excess consisting of salivation, lacrimation, urination, and defecation (SLUD). A full cholinergic syndrome is not seen in this patient. In addition, excessive gastrointestinal symptoms and bronchospasm are not present. Patients who have organophosphate pesticide poisoning typically are

tachypneic from excess pulmonary secretions and bronchospasm; a high temperature is atypical. If necessary, a red blood cell (RBC) count and a plasma cholinesterase level can be obtained. However, even if the cholinesterase results are within normal range, tests should be repeated in a few days to determine the change in values. (See *Case Studies in Environmental Medicine: Cholinesterase-Inhibiting Pesticide Toxicity.*)

Dinitrophenol is present in the insecticide Dinoseb.* Like pentachlorophenol, the pathophysiology of dinitrophenol also involves the uncoupling of oxidative phosphorylation; therefore, poisoning due to these two chemicals would cause similar symptoms. A thorough and careful history would be necessary to exclude the possibility of current contact with the insecticide. Being a botanist by profession and a gardener by hobby, the patient should have an awareness of insecticides he has used, especially those used over a long period of time. Another feature that distinguishes the two chemicals is the staining property. Yellow stains appear on the skin after dermal contact with dinitrophenol; no staining occurs with pentachlorophenol.

(4) To confirm your suspicion of a PCP exposure, you could recommend that the patient's home be tested for airborne levels of PCP. Walls in a room treated with PCP release the chemical into the air, with concentrations reaching 1 nanogram per cubic meter (ng/m^3) of air on the first day after treatment and 160 ng/m^3 on the fourth day. PCP is no longer used in the treatment of wood products intended for use in the interior of residences, but many log cabins and older homes were built before enforcement of regulations that restricted PCP use.

Biologic tests on the patient could also confirm your suspicion. If the exposure is ongoing, urine and blood levels of PCP would be elevated (see *Laboratory Tests*, page 10).

(5) If the patient has PCP poisoning, further laboratory tests could be performed to evaluate the hepatic, renal, and hematologic systems.

(6) Phenol could easily be confused with PCP, especially because they have both been used as disinfectants and preservatives. Phenol is found in many over-the-counter and prescription medications (e.g., ointments, ear and nose drops, cold-sore lotions, mouthwashes, lozenges, gargles, toothache medications, and analgesic rubs) at concentrations of 0.5% to 1.5%. However, the action of phenol and PCP in the body is quite different. PCP primarily acts to uncouple oxidative phosphorylation with resultant hyperthermia. Phenol is primarily a caustic, causing protein denaturation and coagulation.

(7) After initiating acute care (i.e., establishing an intravenous line, administering antibiotics, and instituting cooling treatments), the priority in treating this patient is to prevent further exposure to PCP. This can be accomplished by relocating the patient or by decreasing the level of PCP inside the log cabin. Ensuring adequate ventilation indoors would help, and application of a barrier wood finish such as clear polyurethane to the indoor surfaces of the log cabin would decrease volatilization of the PCP.

* Use of trade names is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services or the Public Health Service.

Posttest and Credits

Continuing education credit is available to health professionals who use this monograph and complete the posttest. The criterion for awarding continuing medical education (CME) credits and continuing education units (CEU) is a posttest score of 70% or better.

The Centers for Disease Control and Prevention (CDC) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to sponsor continuing medical education for physicians, and by the International Association for Continuing Education and Training (IACET) to sponsor continuing education units for other health professionals.

The Agency for Toxic Substances and Disease Registry, in joint sponsorship with CDC, is offering 1 hour of CME credit in Category 1 of the Physician's Recognition Award of the American Medical Association and 0.1 hour of CEU for other health professionals upon completion of this monograph.

In addition, the series *Case Studies in Environmental Medicine* has been reviewed and is acceptable for credit by the following organizations:

The **American Academy of Family Physicians (AAFP)**. This program has been reviewed and is acceptable for 1 prescribed hour by the American Academy of Family Physicians. (Term of Approval: beginning January 1992.) For specific information, please consult the AAFP Office of Continuing Medical Education.

The **American College of Emergency Physicians (ACEP)**. Approved by the American College of Emergency Physicians for one hour per issue of ACEP Category I credit.

The **American Osteopathic Association (AOA)**. AOA has approved this issue for 1 credit hour of Category 2-B credit.

The **American Association of Occupational Health Nurses (AAOHN)**. AAOHN has approved this program for 1.0 contact hours. Applicant will receive the assigned code number in the award letter.

The **American Board of Industrial Hygiene (ABIH)**. ABIH has approved this program for 0.5 certification maintenance (CM) point per 3 Case Studies. The CM approval number is 2817.

To receive continuing education credit (CME or CEU), complete the Posttest on page 17 in the manner shown in the sample question below. **Circle all correct answers.**

Which of the following is known to precipitate migraine headaches?

(a) fatigue
(b) alcohol
c. grapefruit
(d) sunlight
e. sleep

After you have finished the Posttest, please transfer your answers to the answer sheet on the inside back cover and complete the evaluation on the lower half of that page. Fold, staple, and mail the inside back cover to Continuing Education Coordinator, Agency for Toxic Substances and Disease Registry, Division of Health Education, E33, 1600 Clifton Road, Atlanta, GA 30333. Your confidential test score will be returned with an indication of where the correct answers can be found in the text. Validation of earned CME credit and CEU will also be forwarded to participants, and their names, if requested, will be placed on the mailing list to receive other issues in the *Case Studies in Environmental Medicine* series.

POSTTEST: PENTACHLOROPHENOL

Circle **all** correct answers. Record your answers on page 19.

1. In the past, pentachlorophenol (PCP) has been contaminated with
   a. dibenzodioxins
   b. dibenzofurans
   c. dinitrophenols
   d. benzene
   e. chlorophenoxyphenols

2. Which of the following have an increased risk of PCP exposure?
   a. electric utility-line workers
   b. sawmill workers
   c. carpenters
   d. occupants of log cabins
   e. aircraft mechanics

3. Which of the following statements about PCP are true?
   a. It is lipophilic and accumulates in adipose tissue to a large extent.
   b. It is eliminated primarily via the feces as a result of biliary excretion.
   c. Its principal routes of exposure are inhalation and dermal absorption.
   d. It is highly protein bound in the plasma.
   e. It undergoes oxidative metabolism in the liver.

4. Which of the following are potential signs and symptoms of acute PCP poisoning?
   a. cool, clammy skin
   b. hyperthermia
   c. SLUD syndrome (salivation, lacrimation, urination, defecation)
   d. muscle twitching and tremors
   e. metabolic acidosis

5. Which of the following have an important role in the management of acute PCP exposure?
   a. decontamination
   b. pharmacotherapy for seizures
   c. aggressive cooling of the patient
   d. Dantrolene
   e. Seldane

6. Which of the following may be precipitating factors for hyperthermia secondary to PCP exposure?
   a. interference with protein binding in plasma
   b. anticholinergic medication
   c. age
   d. dehydration
   e. acetaminophen use

7. Which of the following laboratory tests are appropriate for a person chronically exposed to PCP?
   a. liver function tests
   b. amylase level
   c. urinalysis
   d. neuropsychologic testing
   e. myoglobin analysis

8. Which of the following may be caused by chronic exposure to technical-grade PCP?
   a. fever
   b. anorexia
   c. fatigue
   d. conjunctivitis
   e. chloracne

Notes

CASE STUDIES IN ENVIRONMENTAL MEDICINE: PENTACHLOROPHENOL TOXICITY

If you wish CME credits or CEU, please indicate your answers to the Posttest questions on page 17 by circling the letters below for the correct answers. Complete the evaluation questionnaire and fill in the information requested on the reverse side. Tear off this last page, fold, staple, and mail to Continuing Education Coordinator, Agency for Toxic Substances and Disease Registry, Division of Health Education, E33, 1600 Clifton Road, Atlanta, GA 30333.

1. a b c d e
2. a b c d e
3. a b c d e
4. a b c d e
5. a b c d e
6. a b c d e
7. a b c d e
8. a b c d e

Evaluation Questionnaire

Please complete the following evaluation by putting a check in the appropriate box.

	Yes	No	Undecided
1. As a result of completing this monograph, I will be able to:			
Explain why pentachlorophenol may be an acute and chronic health health hazard.	☐	☐	☐
Describe the factors that may contribute to pentachlorophenol poisoning.	☐	☐	☐
Identify potential environmental and occupational sources of pentachlorophenol exposure.	☐	☐	☐
Identify evaluation and treatment protocols for persons exposed to pentachlorophenol.	☐	☐	☐
List sources of information on pentachlorophenol.	☐	☐	☐
2. I am more likely to ask patients questions regarding possible environmental exposures as a result of reading this issue.	☐	☐	☐
3. I would recommend this issue to my colleagues.	☐	☐	☐
4. I will keep this issue as a reference.	☐	☐	☐

Comments:_____

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Please send me the following *Case Studies in Environmental Medicine.*

- ☐ Arsenic
- ☐ Asbestos
- ☐ Benzene
- ☐ Beryllium
- ☐ Cadmium
- ☐ Carbon Tetrachloride
- ☐ Chlordane
- ☐ Cholinesterase Inhibitors
- ☐ Chromium
- ☐ Cyanide
- ☐ Dioxins
- ☐ Ethylene/Propylene Glycols
- ☐ Exposure History
- ☐ Gasoline
- ☐ Jet Fuel
- ☐ Lead
- ☐ Mercury
- ☐ Methanol
- ☐ Methylene Chloride
- ☐ Nitrates/Nitrites
- ☐ Pentachlorophenol
- ☐ Polyaromatic Hydrocarbons (PAHs)
- ☐ Polychlorinated Biphenyls (PCBs)
- ☐ Radiation
- ☐ Radon
- ☐ Risk Communication
- ☐ Reproductive and Developmental Hazards
- ☐ Skin Lesions
- ☐ Stoddard Solvent
- ☐ Tetrachloroethylene
- ☐ 1,1,1-Trichloroethane
- ☐ Trichloroethylene
- ☐ Toluene
- ☐ Vinyl Chloride

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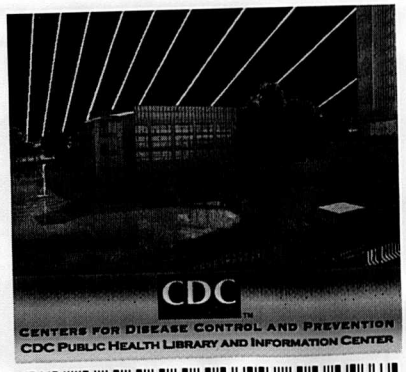
staple or tape



The state of knowledge regarding the treatment of patients potentially exposed to hazardous substances in the environment is constantly evolving and is often uncertain. In this monograph, the Agency for Toxic Substances and Disease Registry (ATSDR) has made diligent effort to ensure the accuracy and currency of the information presented but makes no claim that the document comprehensively addresses all possible situations related to this substance. This monograph is intended as an additional resource for physicians and other health professionals in assessing the condition and managing the treatment of patients potentially exposed to hazardous substances. It is not, however, a substitute for the professional judgment of a health care provider and must be interpreted in light of specific information regarding the patient available to such a professional and in conjunction with other sources of authority.

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