ATSDR

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Case Studies in Environmental Medicine

9 Tetrachloroethylene Toxicity

Environmental ALERT . . .

- ☑ ***Tetrachloroethylene is used mainly as a solvent for dry cleaning and metal degreasing.***
- ☑ ***Like most chlorinated solvents, tetrachloroethylene can cause CNS depression.***
- ☑ ***Chronic exposure to tetrachloroethylene may adversely affect the neurologic system and liver.***

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. The Agency for Toxic Substances and Disease Registry (ATSDR) and the Centers for Disease Control (CDC) designate this continuing medical education activity for 1 credit hour in Category 1 of the Physician's Recognition Award of the American Medical Association and 0.1 continuing education units for other health professionals. See pages 21 to 23 for further information.

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

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 18-19.) The monograph ends with a posttest, which can be submitted to ATSDR for continuing medical education (CME) credit or continuing education units (CEU). See page 21 for further instructions on how to receive these credits.

The objectives of this monograph on tetrachloroethylene are to help you:

- ❑ **Realize why tetrachloroethylene is an acute and chronic health hazard**
- ❑ **Understand the known factors contributing to tetrachloroethylene toxicity**
- ❑ **Assess a patient's environmental or occupational exposure to tetrachloroethylene**
- ❑ **Effectively evaluate and manage tetrachloroethylene-exposed patients**
- ❑ **Utilize a variety of sources to locate further information on tetrachloroethylene**

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 Family Physicians (AAFP), American Academy of Pediatrics (AAP), American College of Emergency Physicians (ACEP), American College of Occupational Medicine (ACOM), American Medical Association (AMA), Association of State and Territorial Health Officials (ASTHO), and the Society of Teachers of Family Medicine (STFM). Final responsibility for the contents and views expressed in this monograph resides with ATSDR.

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Case Study

Headache, decreased concentration, and irritability in a 37-year-old silk screener

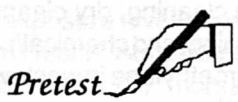
A 37-year-old woman who is 4 months postpartum is seen at your office with complaints of headache, increasing irritability, and difficulty concentrating. She states that she has become impatient and short-tempered with her husband and new child; minor things make her angry. These feelings began about 1 month ago. She is most aware of them in the evenings, when they are sometimes accompanied by a throbbing frontal headache. She has no psychiatric history but admits to drinking 3 ounces of alcohol a day since being married, 4 years ago. She did not drink during the pregnancy and denies using other drugs or medications. She has had no trouble sleeping.

Two weeks ago the patient and her family visited her parents for a week. During that time she felt well; the irritability and headaches subsided. Since coming home last week, however, the symptoms have returned.

The patient is worried that something in the home is causing her symptoms. She reports that the house was sprayed for termites 2 years ago, but she does not remember the name of the fumigant used. Her husband feels fine and has not been ill. Her infant daughter's delivery was uneventful and the baby appears to be developing normally but has been "very fussy" lately. The infant, whom you saw 5 weeks ago for otitis media, is still breast-feeding.

A month ago the patient returned to her job as a word processor, working mornings and relaxing with her hobby, silk screening, in the afternoon. She gets along well with her employer and fellow employees, and the job is not generally stressful. However, she is concerned that a loss in typing accuracy and a decreased ability to concentrate may lead to conflict with her supervisor. The patient has no symptoms of postpartum depression and had no history of headaches before she resumed these activities.

On physical examination you find a slightly overweight woman with blood pressure of 125/85. Pulse is 68 and regular. She is afebriie. Her nail beds are pale. There are no skin rashes, lesions, or stigmata of liver disease. The conjunctiva are mildly injected, but the nares and oral mucosa are not swollen or injected. The thyroid is not enlarged, and no lymphadenopathy is present. There is no focal muscle tension or tenderness. There is no hepatomegaly; examination of the abdomen is unremarkable. Neurologic examination is within normal limits. Recent and distant memory are intact, proverb interpretation is normal, and she is able to do serial 7s. Sensory and motor examination are normal, as are Romberg test and gait. Deep tendon reflexes are normal and symmetrical.



(a) What should be included in this patient's problem list?

(b) What further information would assist in establishing a diagnosis?

(c) What laboratory tests would you order for this patient?

Answers to the Pretest can be found on page 18.

Exposure Pathways

- **Tetrachloroethylene is used mainly as a solvent for dry-cleaning textiles and for cleaning metal parts.**
- **It is also found as an ingredient in a number of consumer products such as fabric cleaners and spot removers.**

Tetrachloroethylene is a clear, colorless, nonflammable liquid having a sweet, fruity odor like chloroform. It is volatile and readily evaporates at room temperature. Tetrachloroethylene is used mainly for textile processing and dry-cleaning fabric (about 53% of total U.S. usage), for degreasing and drying metal parts (10%), and for manufacturing other solvents such as freons (28%). It is used as a solvent and cleaner in consumer formulations including auto brake cleaners, suede protectors, paint removers, water repellents, silicone lubricants, belt lubricants, adhesives, spot removers, wood cleaners, and many products used by hobbyists. Chemical synonyms for tetrachloroethylene include tetrachloroethene, perchloroethylene, 1,1,2,2-tetrachloroethylene, and ethylene tetrachloride. Other commonly used names are perchlor, perc, PCE, tetra, and perclene.

Tetrachloroethylene exposure can result from environmental as well as occupational sources. It is released to air and water by evaporation or fugitive emissions from industrial and dry-cleaning plants, and from landfills where it may be stored. An estimated 80% to 85% of the tetrachloroethylene produced in the United States is eventually released to the environment.

Evaporated tetrachloroethylene collects in the atmosphere and degrades only slowly. Average air levels in the United States range from 0.16 parts per billion (ppb) in rural areas to 1.3 ppb in areas near storage or utilization sites. Some of the tetrachloroethylene in air is carried to the ground through rainwater.

Up to 25% of the water supplies in the United States have detectable levels of tetrachloroethylene, ranging from 0.01 to 1500 ppb, with the highest levels found in aquifers fed by significantly contaminated groundwater. Industrial operations, such as auto engine cleaning, dry cleaning/laundering, aluminum forming, metal finishing, and chemical/plastic manufacturing, may discharge tetrachloroethylene in wastewater at levels exceeding 1 part per million (ppm).

Tetrachloroethylene has been used as an anthelmintic in humans and animals. In soft gelatin capsules, it is effective as an ascaricide for swine, as treatment for stomach worms in sheep, and for the elimination of nematodes (hookworm) in all species including humans. Since more effective and less toxic agents are currently available for these indications, tetrachloroethylene is now seldom used in the United States as a therapeutic agent, and then only for veterinary applications.

Challenge

(1) Additional information for the case study: On questioning, your patient explains that silk screening involves stretching a large piece of cloth across a form, like a picture frame, masking it to create a pattern, then dying the unmasked areas. Before masking the cloth, it must be cleaned. The patient mentions that she just started using a new fabric cleaner about 5 weeks ago. Her cousin, who also enjoys silk screening, assured her it was harmless and the best available. The product is called "Clean Cloth," but the patient can remember little else about it.

Assuming the label on the "Clean Cloth" container does not list the contents, how will you determine the ingredients of this consumer product?

Who's at Risk

An estimated 500,000 workers in the United States may be at risk of exposure to tetrachloroethylene; many of these workers are employed in the 20,000 dry-cleaning establishments in this country. A NIOSH survey of 44 dry-cleaning facilities found air levels of tetrachloroethylene ranging from 4 to 149 ppm in the shop areas and from 0.5 to 3.1 ppm at the front counter. Much higher tetrachloroethylene levels are associated with cleaning spills or replacing dry-cleaning filters. (The current permissible workplace exposure level as promulgated by the Occupational Safety and Health Administration [OSHA] is 25 ppm averaged over an 8-hour workshift.) Increased opportunity for exposure may also be encountered by machinists, plastic extruders, and electronic assemblers, and by workers manufacturing consumer products containing tetrachloroethylene.

Exposures to consumer products containing tetrachloroethylene have led to acute toxicity. Accidental ingestions or spills, and use of products in small, enclosed spaces may place unsuspecting persons at risk. For example, a spot remover containing tetrachloroethylene used to clean a carpet in a poorly ventilated area can produce dangerously high air levels. Clothes, drapes, or other re-

- **Workers in industries such as dry cleaning, machining, and electronics, as well as consumers who use tetrachloroethylene-containing products have an increased likelihood of exposure.**
- **Persons using well water contaminated with tetrachloroethylene can be exposed by inhalation as well as ingestion.**
- **Tetrachloroethylene crosses the placenta and can be found in breast milk; therefore, the fetus and nursing newborn may be at increased risk of adverse effects from maternal exposure.**

cently dry-cleaned fabrics may release tetrachloroethylene for several hours. The death of a teenaged boy has been attributed to tetrachloroethylene intoxication from an inadequately aired sleeping bag dry-cleaned a short time before use, and a patient was reported to develop stupor and coma after inhaling tetrachloroethylene vapors from clothes cleaned in a self-service dry-cleaning machine.

Generally, environmental background levels of tetrachloroethylene in urban air and water are low and have not been known to cause adverse effects. Low levels of tetrachloroethylene were found in the exhaled breath of teachers and children at a kindergarten located near a factory using the chemical, and in the residents of a retirement home located near a former chemical waste dump. Occasionally, well water is contaminated with tetrachloroethylene at significant levels; exposures in these cases can occur by inhaling vapors during bathing or laundering, and by drinking the water.

Data from animal and human studies indicate that tetrachloroethylene crosses the placenta. Although effects are uncertain, this ease of distribution may place the fetus at increased risk. In addition, tetrachloroethylene, like most other chlorinated chemicals, can be transmitted in breast milk, thus subjecting the nursing newborn to continued exposure. In one case report, a nursing mother, who had been repeatedly exposed to tetrachloroethylene fumes during lunch-hour visits with her husband at a dry-cleaning plant, had tetrachloroethylene levels of 300 µg/dL in blood and 1000 µg/dL in breast milk. The nursing infant developed obstructive jaundice, possibly as a result of tetrachloroethylene exposure.

Challenge

(2) The certified poison control center in your region informs you that "Clean Cloth" is 90% tetrachloroethylene and 10% Freon-22 (dichlorodifluoromethane). Might the infant described in the case study be at increased risk? Explain.

Biologic Fate

In humans, about 70% of an inhaled tetrachloroethylene dose is absorbed by the lungs, and about 80% of an oral dose is absorbed by the gut. Tetrachloroethylene penetrates human skin slowly. Once tetrachloroethylene is absorbed, it is readily distributed to all body tissues. Because it is highly lipid-soluble, it tends to concentrate primarily in adipose tissue.

More than 80% of absorbed tetrachloroethylene is eliminated unchanged by the lungs. With minimal physical activity, elimination of tetrachloroethylene from blood occurs in a biphasic pattern. In one study, the average half-life of each phase was 2.6 hours and 33 hours, respectively. The average half-life of tetrachloroethylene in adipose tissue is about 72 hours.

Less than 2% of absorbed tetrachloroethylene is metabolized in the liver to trichloroacetic acid and trichloroethanol, which are then excreted in the urine. The rate of urinary elimination is slower than the exhalation rate, with urinary biologic half-lives ranging from 12 to 55 hours for the first phase, and 100 to 200 hours for the second phase. Studies of dry-cleaning shop workers have shown that urinary metabolite levels increase linearly with air concentrations up to 100 ppm tetrachloroethylene, then level off at higher concentrations. This indicates the saturability of the tetrachloroethylene metabolic pathways.

- **Tetrachloroethylene does not bioaccumulate in the food chain.**
- **Most absorbed tetrachloroethylene is excreted unchanged in the breath; a small amount is metabolized in the liver and excreted in urine as trichloroacetic acid and trichloroethanol.**
- **The elimination of tetrachloroethylene and its metabolites appears to be biphasic, with a rapid first phase (hours), and a second slow phase (days).**

(3) How could you determine if a patient has been exposed to tetrachloroethylene?

Physiologic Effects

Exposure to tetrachloroethylene has resulted in effects on the central nervous system (CNS), skin, mucous membranes, eyes, lungs, liver, and kidney. CNS effects have been noted most frequently.

Acute Exposure

- **As with most chlorinated solvents, acute exposure to tetrachloroethylene primarily affects the CNS and causes skin, throat, and eye irritation.**

Acute exposure to tetrachloroethylene at air levels of 75 to100 ppm causes irritation of the eyes and upper respiratory tract. Minor CNS effects have also been observed with acute inhalation exposures from 100 to 300 ppm. At the latter levels, the Romberg test may be positive and results of certain coordination and behavioral tests may be abnormal. At higher air levels, unconsciousness can occur.

Acute tetrachloroethylene ingestion rarely occurs, but as much as 500 mg/kg did not cause death in one case, and, in another case, CNS depression was noted with ingestion of 4.2 to 16 g. Up to 16 g has been ingested without causing liver or renal injury.

Chronic Exposure

- **Besides affecting the CNS and skin, tetrachloroethylene may adversely affect the liver, kidneys, and possibly the heart.**

Chronic exposure to tetrachloroethylene may have adverse effects on the skin and hepatic, renal, and nervous systems. Although tetrachloroethylene causes cancer in animals, it has not been established as a human carcinogen. Nevertheless, based on the weight of evidence in animals, the U.S. Environmental Protection Agency (EPA) classifies tetrachloroethylene as a probable human carcinogen. Insufficient data are available to judge whether tetrachloroethylene adversely affects reproductive and developmental outcomes in humans.

Nervous System Effects

- **CNS effects are generally reversible on cessation of exposure.**

Persons chronically exposed to tetrachloroethylene may experience short-term memory deficits, ataxia, irritability, disorientation, and sleep disturbances. In one case, the owner of a dry-cleaning shop in business for 30 years was diagnosed with progressive dementia. His serum tetrachloroethylene level was 75 µg/dL, whereas serum levels rarely exceed 5 µg/dL in the general population.The patient's short-term memory impairments gradually cleared over several months after exposure to tetrachloroethylene ceased. Some patients may be mistakenly diagnosed with Alzheimer's disease or other CNS disorders when, in fact, they have a preventable and possibly reversible condition.

Hepatic and Renal Effects

- **Hepatic and renal toxicity may occur in humans exposed to tetrachloroethylene.**

Tetrachloroethylene is considered a weak hepatotoxin based on case reports of human exposure. Hepatitis, cirrhosis, liver cell necrosis, hepatomegaly, and elevated liver function indices have been noted. Most reported cases are due to accidental exposures or deliberate abuse of unknown dose and duration. Mild transient increases in serum transaminase values have occurred as a result of a severe, brief exposure in adults; organ dysfunction has been noted only after months of exposure at levels in excess of 100 ppm. In animal studies, intermittent exposures to air levels as low as 9 ppm tetrachloroethylene have produced irreversible hepatic injury.

Nonproliferative kidney lesions are characteristic of other chlorinated compounds with similar chemical structure; thus, tetrachloroethylene should be regarded as a possible nephrotoxic agent in humans. Nephrotoxicity or hepatotoxicity would not be expected, however, from exposure at environmental levels or at the current permissible workplace level.

Cardiac Effects

- **Tetrachloroethylene may affect the heart; however, no deaths due to cardiotoxicity have been reported in workers.**

The cardiac effects of tetrachloroethylene in animals have been studied extensively. In some anesthetized species, high levels of tetrachloroethylene increased the vulnerability of the ventricles to epinephrine-induced extra-systoles, bjgeminal rhythms, and tachycardia. In one study, ventricular dysrhythmias occurred in approximately 30% of the anesthetized animals after injection of tetrachloroethylene alone. The effects of agents with anesthetic properties, however, may be indistinguishable from the effects of anesthesia-related hypoxia and acidosis.

Tetrachloroethylene may be associated with cardiotoxicity in some persons. One case has been noted of a dry cleaner who had symptomatic ventricular ectopy that temporally correlated with elevated plasma tetrachloroethylene levels during work. He may have been particularly sensitive to tetrachloroethylene, however, since no similar cases have been reported.

Reproductive and Developmental Effects

- **No teratogenic effects of tetrachloroethylene have been found in experimental animals.**

Tetrachloroethylene did not cause birth defects in exposed rats and mice. It was associated with lower fetal weights, but only at exposure levels that were also toxic to the dams. The few studies of tetrachloroethylene's effects on human reproductive outcomes are inconclusive, although they suggest that adverse reproductive or developmental effects might occur.

Male workers exposed to tetrachloroethylene have not displayed reproductive effects. Maternally absorbed tetrachloroethylene is known to cross the placenta and can also be transmitted to the nursing newborn in milk. Women who regularly work with the chemical should avoid excessive exposures and should not breast-feed. The 6-week-old infant described on page 4, who developed obstructive jaundice and hepatomegaly, improved clinically after breast-feeding was discontinued; liver function was normal during 2 years of follow-up.

Carcinogenic Effects

- **Conclusive proof of the carcinogenic potential of tetrachloroethylene in humans is lacking.**

Some epidemiologic studies of dry-cleaning workers have suggested a possible association between chronic tetrachloroethylene exposure and increased cancer risk. Studies have reported lymphoma and various cancers of the lung, larynx, skin, cervix, uterus, liver, kidney, and bladder. The results have been judged inconclusive because these studies were based on inadequate information of the degree of exposure and investigators were unable to control for smoking, socioeconomic status, and exposure to other solvents.

In studies using mice or rats, high-dose oral administration of tetrachloroethylene was associated with an increased incidence of hepatocellular carcinoma, and inhalation exposure was associated with leukemia, renal tubular cell adenomas, and adenocarcinomas. Data from animal studies, together with supporting data on tetrachloroethylene mutagenicity, constituted a sufficient level of evidence for EPA to classify tetrachloroethylene as an animal carcinogen and a probable human carcinogen.

Challenge

(4) What will you tell your patient regarding the hazards of tetrachloroethylene?

Clinical Evaluation

History and Physical Examination

The physician should ask about previous occurrences of similar symptoms. If a temporal association between symptoms and exposure to certain products is suspected, an attempt should be made to identify the specific chemical ingredients involved. If the product label does not list the chemical ingredients, the regional poison control center may maintain a list of ingredients in consumer and proprietary products. In occupational exposures, the employer or manufacturer is required by law to provide a material safety data sheet (MSDS), which lists the chemical ingredients and describes their potential toxicity.

- **The physician should attempt to establish a temporal relationship between symptoms and exposure to tetrachloroethylene.**

- **Physical examination should include skin, ENT, liver, kidneys, and CNS.**

It will be helpful to know if other family members or coworkers have similar symptoms. It is also important to note the time of last exposure to a suspected chemical since a temporal relationship between onset of symptoms and work or other activity may provide important clues. One should also evaluate general health and question the patient regarding alcohol and drug use.

Eyes, nose, throat, and skin should be examined carefully for inflammation or irritation. The conjunctiva may be injected, and nasal mucosa, may be injected and swollen. Repeated inhalation exposures to tetrachloroethylene can cause defatting of nasal mucosa, leading to a friable condition with drying, cracking, or bleeding. Skin contact may cause dermatitis by irritation and defatting.

A complete neurologic evaluation should be performed with special attention to memory, gait, and balance. Short-term memory loss, if associated with tetrachloroethylene exposure, is generally transient. In patients with acute exposures, the Romberg balance test has been positive. The patient should be examined for hepatomegaly. Vital signs should be recorded, especially abnormalities of heart rate or rhythm. Patients should be assessed for costovertebral angle tenderness, and the history should include any urinary abnormalities such as hematuria.

Signs and Symptoms

Acute Exposure

Background levels of tetrachloroethylene in air, water, and food have not been associated with symptoms. The odor threshold of tetrachloroethylene is reported to be from 5 to 50 ppm; symptoms

- **Odor may not provide adequate warning of toxic tetrachloroethylene levels.**

Effects of acute inhalation exposure include mucous membrane irritation and CNS depression.

typically do not occur until approximately 75 ppm. Odor warning is not always reliable, however, because some people have a higher threshold of detection, and acclimatization to tetrachloroethylene can occur.

The principal symptoms of acute inhalation exposure are eye and upper airway irritation (at 75 to 100 ppm) and CNS depression (at 100 to 300 ppm). Eye instillation can lead to corneal burns and conjunctivitis; skin contact may result in inflammation or chemical burns. If tetrachloroethylene contacts fire or a hot metal surface, it can produce irritating or poisonous gases such as chlorine and phosgene.

The onset, intensity, and duration of symptoms can vary among identically exposed persons. The variability of toxicity is influenced by many factors such as respiratory rate, target organ sensitivity, body fat content, and general health. CNS symptoms can be similar to those of ethanol inebriation. Pulmonary edema has occurred in one laundry worker found unconscious after exposure to tetrachloroethylene vapor.

Symptoms associated with acute high-level tetrachloroethylene exposure may include the following:

Nervous system

Euphoria
Headache
Dizziness
Light-headedness
Sleepiness
Forgetfulness
Irritability
Slurred speech
Confusion
Loss of coordination
Loss of consciousness

Gastrointestinal

Nausea

ENT

Eye and nose irritation
Upper airway irritation and cough

Chronic Exposure

Chronic exposure may affect the skin, and neurologic and hepatic systems.

Mild CNS symptoms are often reported in conjunction with exposure to tetrachloroethylene-containing household products in confined spaces, and with exposure in industrial settings. Workers' symptoms have included persistent headache, short-term memory deficits, ataxia, irritability, disorientation, and sleep distur-

bances. Evidence in volunteers and exposed workers indicates that levels of 25 ppm or less do not produce neurologic deficits or behavioral performance impairment.

The liver is the primary target organ in animals exposed chronically to tetrachloroethylene. In humans, chronic exposure has led to hepatitis and elevated transaminase levels (SGOT or AST and SGPT or ALT). Death due to hepatorenal failure has been reported only as a result of tetrachloroethylene abuse.

Dysrhythmia was noted in one worker exposed occupationally to tetrachloroethylene; no sudden deaths have been reported. Tetrachloroethylene's defatting action on skin may cause dermatitis, thereby predisposing the skin to infection.

Laboratory Tests

Direct Biologic Indicators

In exposed persons, tetrachloroethylene may be measured in expired air and blood; its metabolite, trichloroacetic acid, may be measured in blood and urine. If the cause of symptoms is questionable, direct biologic testing may be warranted. However, other chemical exposures, such as to 1,1,1-trichloroethane and trichloroethylene, can also result in the presence of trichloroacetic acid in blood and urine. Trichloroethanol, another metabolite of tetrachloroethylene and trichloroethylene, has been reported, but not consistently, in urine of tetrachloroethylene-exposed workers. Trichloroethanol and trichloroacetic acid can also be found in patients taking chloral hydrate.

- **Tetrachloroethylene itself may be measured in breath and blood; its metabolites can be measured in blood and urine.**

To measure tetrachloroethylene in blood or expired air, samples should be collected within 16 hours after exposure; urine tests will remain positive up to 5 days after exposure, depending on the dose. Few laboratories perform these specialized tests; regional poison control centers may be able to identify such facilities. The method of sampling and sample storage must be coordinated with the laboratory to ensure proper specimen collection and processing. The laboratory should provide reference values appropriate for the analytical method used, if they exist. Recording the time of sample collection relative to the last exposure is critical to interpretation of results.

Expired air and blood tetrachloroethylene levels and urine trichloroacetic acid levels have been linearly correlated with ambient air concentrations up to 100 ppm. In workers, a trichloroacetic acid level of 7 mg/L in urine obtained at the end of the workweek was

found to correlate with exposure to an average of 50 ppm tetrachloroethylene for 1 week. The same exposure level will result in approximately 100 µg/dL tetrachloroethylene in blood drawn 16 hours after the last work shift of the week. Increased physical activity during exposure can result in higher levels.

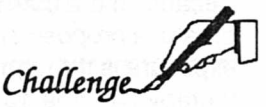
Indirect Biologic Indicators

- **Significant exposure to tetrachloroethylene may result in elevated values of renal and liver function tests.**

Although tetrachloroethylene may cause upper airway irritation and coughing, the chest X ray or pulmonary function test will probably be normal. In general, results of routine laboratory tests, including renal and liver function tests, will also be normal unless the patient has had a significant exposure and has concurrent neurologic symptoms.

Transient elevation of transaminase levels has been reported in tetrachloroethylene exposures, but frank hepatic necrosis has not been documented. If a known acute exposure to tetrachloroethylene results in CNS symptoms such as syncope, then liver function tests, BUN, serum creatinine, and urinalysis should be obtained immediately to establish baseline. Testing should be repeated after several days to monitor for possible effects. Liver function tests should include SGOT (AST), SGPT (ALT), lactic dehydrogenase (LDH), bilirubin, and alkaline phosphatase. If levels are mildly elevated, tests should be repeated in several weeks to document return to baseline. If levels remain elevated, other causes of hepatic dysfunction should be investigated.

The value of a neuropsychologic evaluation for differentiating between organic and functional impairment is controversial, especially when no baseline evaluation is available. The tests, however, may be useful when comparing an exposed occupational population to a control group. Although neurologic tests provide "soft" data, they may be used to raise suspicion of cognitive impairments that are not evident on mental status testing, or as a baseline for follow-up.



(5) What other history will help in determining if the neurologic symptoms of the patient described in the case study are due to "Clean Cloth"?

_____

_____

(6) The patient asks why her cousin, who uses "Clean Cloth" for the same purpose, has not been ill. What can you tell her?

_____

_____

(7) The patient's laboratory tests show urinary trichloroacetic acid of 4.2 mg/L immediately after a 1-week exposure and a slightly elevated SGOT and SGPT. How do you interpret these results?

_____

_____

Treatment and Management

Acute Exposure

No specific treatments are available for acute tetrachloroethylene exposures. Data from humans are insufficient to determine an ingestion level at which emesis should be induced. If a gag reflex is not apparent, emetics should not be administered because aspiration of gastric contents could result. Gastric lavage may be useful in recent, large ingestions. Although charcoal and cathartics may be given, their efficacy is not proven.

Contaminated clothing should be removed without endangering health care personnel. Supportive care directed to adequate ventilation and circulation should be provided. Moderately to severely exposed patients should have cardiac monitoring for potential dysrhythmias, and oxygen should be administered if respiratory depression has occurred.

- **There is no antidote for tetrachloroethylene toxicity; supportive measures should be administered.**
- **In a patient who ingested tetrachloroethylene, controlled hyperventilation therapy was apparently successful.**

Because more than 80% of tetrachloroethylene is eliminated in the breath, a proposed method of clearing it from the body in an acute exposure is through controlled hyperventilation. Hyperventilation therapy (volume 10 L/min) was used on a comatose 6-year-old, 2 hours after the child ingested 8 to 10 mL of pure tetrachloroethylene. The initial tetrachloroethylene blood level was 2150 µg/dL. On the fifth day, when hyperventilation was terminated, the blood level was less than 100 µg/dL. The child completely recovered. The effectiveness of hyperventilation in tetrachloroethylene overdose, however, has not been validated. Without experimental controls, the extent to which hyperventilation contributed to the boy's recovery remains uncertain.

CNS symptoms due to acute tetrachloroethylene inhalation exposure are transient but may linger for hours after exposure ceases. Patients usually recover rapidly without permanent neurologic sequelae if hypoxia and shock have been prevented.

Chronic Exposure

❑ **Long-term management requires reduction or elimination of exposure.**

Symptoms related to chronic exposure tend to worsen during exposure and improve over a weekend, on vacation, or with a job transfer. If there is no clear association between symptoms and exposure, other etiologies should be considered.

For persons with tetrachloroethylene toxicity, the level of exposure either must be reduced or the source eliminated. Substitution of an agent less hazardous than tetrachloroethylene may be feasible. It is important that substances containing tetrachloroethylene be handled in well-ventilated areas. High levels of exposure can occur during clean-up of contaminated equipment and spills, and may require use of an approved full facepiece self-contained breathing apparatus (SCBA) or similar device. Procedures for cleaning up spills should be established in advance. All containers of liquid tetrachloroethylene should be capped; rags soaked with tetrachloroethylene should be stored in sealed containers.

(8) What recommendations can you make if the patient wishes to continue using "Clean Cloth"?

Standards and Regulations

Workplace

Air

OSHA has a maximum permissible exposure limit (PEL) in workplace air of 25 ppm measured as an 8-hour time-weighted average (TWA). This regulatory level was reduced from 100 ppm in 1989 (Table 1).

❑ **The current OSHA 8-hour TWA for tetrachloroethylene is 25 ppm.**

Table 1. Standards and regulations for tetrachloroethylene

Agency*	Focus	Level	Comments
ACGIH	Air -Workplace	50 ppm	Advisory; TLV-TWA†; STEL§ of 200 ppm
NIOSH	Air -Workplace	N/A	Advisory; lowest feasible level
OSHA	Air -Workplace	25 ppm	Regulation; PEL¶ over 8-hour workday
EPA	Air-Environment	None	Regulation under development; due early 1991
	Water-Environment	None	Regulation; proposed 5 ppb to take effect winter 1990

* ACGIH = American Conference of Governmental Industrial Hygienists; EPA = Environmental Protection Agency; NIOSH = National Institute for Occupational Safety and Health; OSHA = Occupational Safety and Health Administration

† TLV-TWA (Threshold Limit Value–Time-Weighted Average) = time-weighted average concentration for a normal 8-hour workday and 40-hour workweek to which nearly all workers may be repeatedly exposed.

§ STEL (Short-Term Exposure Limit) = usually a 15-minute sampling period.

¶ PEL (Permissible Exposure Limit) = highest level of tetrachloroethylene in air to which a worker may be exposed, averaged over an 8-hour workday.

- **NIOSH considers tetrachloroethylene a potential carcinogen and recommends exposure in the workplace be reduced to the lowest possible level.**

The National Institute for Occupational Safety and Health (NIOSH) in 1976 recommended a maximum 8-hour TWA of 50 ppm with a ceiling of 100 ppm, as determined by 15-minute sampling periods. This recommended standard was based on the reported level at which CNS disturbances occurred. In 1978, NIOSH recommended that tetrachloroethylene be handled in the workplace as a potential human carcinogen and that occupational exposure be reduced to the lowest feasible level.

The American Conference of Governmental Industrial Hygienists (ACGIH) has established the following biologic exposure indices (BEIs): 10 ppm tetrachloroethylene in end-exhaled air, sample collected after a minimum of 2 consecutive workdays with exposure; 100 µg/dL tetrachloroethylene in blood, specimen collected after at least 2 consecutive workdays with exposure; and 7 mg/L trichloroacetic acid in urine, specimen collected at end of the workweek. A BEI is a recommended "warning level" and not necessarily a threshold that should not be exceeded. The BEI may be underprotective or overprotective because of individual susceptibility due to the influence of variables such as body habitus, level of activity, and mixed exposures.

Environment

Air

- **EPA intends to propose air emission standards for tetrachloroethylene in early 1991.**

EPA intends to propose air emission standards for specific tetrachloroethylene sources in early 1991. These sources will include dry cleaners, chemical manufacturers, and degreasers (solvent cleaning operations).

Water

- **EPA has proposed a drinking water maximum contaminant level (MCL) of 5 ppb.**

At present EPA has no standard for tetrachloroethylene in drinking water, but has proposed regulations to take effect in the winter of 1990. The MCL proposed by EPA is 5 ppb; the maximum contaminant level goal (MCLG) proposed is zero.

Challenge

(9) What authorities should be notified if you believe a product is being used improperly in an industrial setting? By a large number of hobbyists?

Suggested Reading List

General

Koppel C, Arndt I, Arendt U, Koeppe P. Acute tetrachloroethylene poisoning--blood elimination kinetics during hyperventilation therapy. J Toxicol Clin Toxicol 1985;23:103-15.

Materna BL. Occupational exposure to perchloroethylene in the dry cleaning industry. Am Ind Hyg Assoc J 1985;46(5):268-73.

Ohtsuki T, Sato K, Koizumi A, Kumai M, Ikeda M. Limited capacity of humans to metabolize tetrachloroethylene. Int Arch Occup Environ Health 1983;51:381-90.

Stewart RD, Baretta ED, Dodd HC, Torkelson TR. Experimental human exposure to tetrachloroethylene. Arch Environ Health 1970;20:225-9.

Verberk MM, Scheffers TML. Tetrachloroethylene in exhaled air of residents near dry-cleaning shops. Environ Res 1980;21:432-7.

Reproductive Toxicity

van der Gulden JW, Zielhuis GA. Reproductive hazards related to perchloroethylene: a review. Int Arch Occup Environ Health 1989;61:235-42.

Carcinogenicity

Brown DP, Kaplan SD. Retrospective cohort mortality study of dry cleaner workers using perchloroethylene. J Occup Med 1987;29:535-41.

Smith EM, Miller ER, Woolson RF, Brown CK. Bladder cancer risk among laundry workers, dry cleaners, and others in chemically-related occupations. J Occup Med 1985;27:295-7.

Biologic Monitoring

American Conference of Governmental Industrial Hygienists. Documentation of the threshold limit values and biological exposure indices. 5th ed. Cincinnati: American Conference of Governmental Industrial Hygienists, 1986.

Ghittori S, Imbriani M, Pezzagno G, Capodaglio E. Urinary concentration of solvents as a biological indicator of exposure. Proposal for the "Biological Equivalent Exposure Limit" for 9 solvents. Am Ind Hyg Assoc J 1987;48:786-90.

Imbriani M, Ghittori S, Pezzagno G, Capodaglio E. Urinary excretion of tetrachloroethylene (perchloroethylene) in experimental and occupational exposure. Arch Environ Health 1988;43:292-8.

Lauwerys R, Herbrand J, Buchet JP, Bernard A, Gaussin J. Health surveillance of workers exposed to tetrachloroethylene in dry-cleaning shops. Int Arch Occup Environ Health 1983;52:69-77.

Monster A, Regouin-Peeters W, van Schijndel A, van der Tuin J. Biological monitoring of occupational exposure to tetrachloroethene. Scand J Work Environ Health 1983;9:273-81.

Related Government Documents

Agency for Toxic Substances and Disease Registry. Toxicological profile for tetrachloroethylene. Atlanta: US Department of Health and Human Services, Public Health Service, 1989.

Centers for Disease Control. Worker exposure to perchloroethylene in commercial dry-cleaning operations—United States. MMWR 1983;32:269-71.

Environmental Protection Agency. Health assessment document for tetrachloroethylene (perchloroethylene): final report. Washington, DC: US Environmental Protection Agency, Office of Health and Environmental Assessment, 1985. Report no. EPA/600/8-82/005F; NTIS report no. PB85-249705.

Environmental Protection Agency. Addendum to the health assessment document for tetrachloroethylene (perchloroethylene), updated carcinogenicity assessment for tetrachloroethylene (perchloroethylene, PERC, PCE). Research Triangle Park, NC: US Environmental Protection Agency, Office of Health and Environmental Assessment, 1986. Report no. EPA/600/8-82/005FA.

Answers to Pretest and Challenge Questions

Pretest

Pretest can be found on page 1.

(a) Your patient is 4 months postpartum, has transient headaches, irritability, decreased ability to concentrate, slightly impaired coordination, and possible alcoholism.

(b) It would help to have more information about the history of her headaches and her silk screening hobby and an accurate history of her current drinking pattern.

(c) Since the patient is postpartum and possibly consumes alcohol in excess, you should rule out anemia and check renal and hepatic functions. A complete blood count, urinalysis, BUN, serum creatinine, and liver function tests would be appropriate.

Challenge

Challenge questions begin on page 3.

(1) The quickest way to identify the ingredients in "Clean Cloth" may be to call your regional poison control center. If this is unsuccessful, ask the patient to obtain a material safety data sheet (MSDS) for "Clean Cloth" from the store that sells it or the manufacturer's sales representative or chemist. (The MSDS will list ingredients in the product and describe their toxicity.)

(2) Yes, maternal exposure to tetrachloroethylene could result in the chemical being transmitted to the nursing infant since the solvent selectively concentrates in breast milk. In addition, the infant may be exposed through inhalation if she is nearby when the fabric is being cleaned.

(3) As is discussed in the Laboratory Tests section, direct indications of tetrachloroethylene exposure can be obtained by measuring levels in breath or blood and by measuring metabolites in urine. Perhaps a first step would be to halt the exposure and determine if the symptoms resolve.

(4) You should inform your patient of the adverse effects of acute and chronic exposure to tetrachloroethylene and advise her and her cousin to use a well-ventilated area when cleaning cloth during silk-screening. You should also review the potential long-term risks, particularly to nursing infants.

(5) Questions about symptoms and temporal association of the use of "Clean Cloth" may reveal a direct connection. The type and amount of ventilation also may have an effect. (Your questioning reveals that the patient sprays the cloth in late afternoon in a small garage and keeps the door closed to prevent dust from entering. She recalls that one day last week when it was hot, she felt particularly ill after spraying the cloth.)

(6) You should review the factors that may reduce the cousin's actual exposure. For example, the cousin may work outdoors or in a better ventilated area, or she may not leave rags soaked with the compound lying about, etc. You could also discuss individual variability as a reason why some people become ill and others do not after similar exposures.

(7) The urinary trichloroacetic acid level indicates an average ambient air exposure of about 30 ppm tetrachloroethylene (calculated using the occupationally based ratio on page 11). While this level indicates definite exposure, it may not be high enough to cause her symptoms; however, the patient could have been periodically exposed to short-term levels much higher than this average level, which could have caused her symptoms.

Although not relevant here, the linear correlation between urinary trichloroacetic acid and tetrachloroethylene exposure levels breaks down when the exposure is above 100 ppm tetrachloroethylene. The plateau effect resulting from saturation of the tetrachloroethylene metabolic pathway limits the effectiveness of the assay when the ambient level is above 100 ppm.

The slightly elevated levels of SGOT and SGPT are inconclusive for tetrachloroethylene exposure because of the confounding factor of alcohol consumption. An SGOT:SGPT ratio greater than 1 (i.e., SGOT greater than SGPT) tends to support an alcoholic etiology; a ratio less than 1 (i.e., SGOT less than SGPT) supports toxic, infectious, or other etiologies. The patient should be advised to reduce alcohol consumption and be counseled regarding alcoholism if this is a problem. Liver function tests should be repeated in several months.

(8) It would be preferable to seek a less toxic replacement. However, if the patient insists on continuing with "Clean Cloth," you should advise her to get proper industrial hygiene consultation or other professional assistance. The local or state health department may be able to provide some information.

Your patient would be well-advised to avoid breast feeding while exposed to tetrachloroethylene. Should she find a "Clean Cloth" alternative that has no chlorinated solvents, the tetrachloroethylene presently in her milk can be eliminated in several days if she continues to pump her breasts.

(9) OSHA has regulatory responsibility for the workplace and should be notified if employees may be dangerously exposed. You could also request that NIOSH initiate a Health Hazard Evaluation of the workplace. A product with hazardous potential used by a number of hobbyists would be reported to the local or state health department.

Sources of Information

More information on the adverse effects of tetrachloroethylene and the treatment and management of tetrachloroethylene-exposed persons can be obtained from ATSDR, your state and local health departments, and university medical centers. *Case Studies in Environmental Medicine: Tetrachloroethylene Toxicity* is one of a series. For other publications in this series, please use the order form on the back cover. For clinical inquiries, contact ATSDR, Division of Health Education, Office of Director, at (404) 639-0730.

Posttest

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

The Centers for Disease Control (CDC) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to sponsor continuing medical education for physicians, and by the Council on the Continuing Education Unit (CCEU) 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 credit hour of continuing medical education (CME) credit in category 1 of the Physician's Recognition Award of the American Medical Association and 0.1 hour of continuing education units (CEU) for other health professionals upon completion of this monograph.

The American College of Emergency Physicians (ACEP) has approved this program for 1 hour of ACEP Category 1 credit.

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

To receive continuing education credit (CME or CEUs), complete the Posttest on page 22 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 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 CEUs 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: TETRACHLOROETHYLENE

Circle **all** correct answers and transfer your answers to page 23.

1. Which of the following persons have an increased likelihood of tetrachloroethylene exposure?
   a. machinists and metal degreasers
   b. dry cleaning workers
   c. tobacco farmers
   d. breast-fed infants of exposed mothers
   e. tree sprayers

2. Which of the following statement(s) about tetrachloroethylene is (are) true?
   a. it is well absorbed from the lungs
   b. an ingested dose can result in gangrene
   c. most of an absorbed dose is metabolized in the liver
   d. most of an inhaled dose is eliminated in urine
   e. it is rapidly exhaled unchanged

3. Central nervous system effects due to tetrachloroethylene
   a. can occur in the absence of liver toxicity
   b. are enhanced in a person exercising while exposed to tetrachloroethylene
   c. are due to trichloroacetic acid, a major metabolite of tetrachloroethylene
   d. can be treated by administering Inderal
   e. can result in a positive Romberg test at high exposure levels

4. CNS effects of *chronic* inhalation exposure to tetrachloroethylene include
   a. paranoid psychosis
   b. dysesthesia
   c. disorientation
   d. tactile hallucinations
   e. reversible short-term memory deficits

5. Which of the following products contain tetrachloroethylene?
   a. shoe polish
   b. home rug cleaners
   c. laundry soaps
   d. fabric cleaners
   e. insect repellents

6. Patients with *acute* tetrachloroethylene overexposure can have
   a. slurred speech
   b. memory deficit
   c. severe hepatic necrosis
   d. jaundice
   e. upper respiratory irritation

7. Renal failure after acute tetrachloroethylene exposure is probably
   a. caused by an excess of HCl resulting from the solvent's metabolism
   b. caused by a rise in urobilinogen
   c. a result of vascular collapse following CNS depression
   d. associated with ensuing brain hemorrhage
   e. a direct result of tetrachloroethylene's dermal effects

8. Specific treatment(s) for acute inhalation of tetrachloroethylene include(s)
   a. oxygen
   b. indwelling bladder catheter
   c. activated charcoal
   d. emesis
   e. ethanol administered intravenously

CASE STUDIES IN ENVIRONMENTAL MEDICINE: TETRACHLOROETHYLENE

If you wish CME credits or CEUs, please indicate your answers to the Posttest questions on page 22 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.

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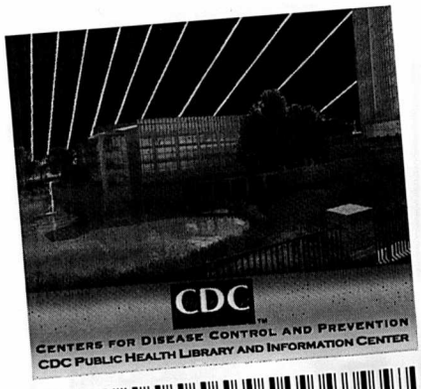

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