TSDR

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Case Studies in Environmental Medicine

6 Trichloroethylene Toxicity

Environmental ALERT...

- ☑ ***Trichloroethylene (TCE) is a common industrial solvent and contaminant of hazardous waste sites, groundwater, and drinking water.***
- ☑ ***TCE is a CNS depressant and a suspected hepatotoxin in humans.***
- ☑ ***EPA considers TCE an animal carcinogen and a potential cancer hazard to humans.***

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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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 19-20.) 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 trichloroethylene are to help you:

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

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Case Study

Concerns of a young family exposed to TCE-contaminated drinking water

Your practice is in a suburban community with a number of high-technology industries. A couple for whom you have been the family physician asks for an appointment to discuss their daughter's illnesses and a matter of concern to them.

During the initial consultation, the mother reports that they are living in an area supplied by municipal well water. They have recently received a notice from the municipal water district stating that their drinking water contains 100 parts per billion (ppb) trichloroethylene (TCE), and as a precaution, they are being supplied with bottled drinking water until an alternative well can be put into service. The notice indicates that the well water is suitable for bathing and laundering. The father interjects that he is familiar with TCE; it is used in the electronics plant where he works.

The daughter, aged 4, has had a number of ear infections during her first 2 years, culminating in a myringotomy at age 3. Follow-up by an ENT specialist has shown normal hearing. Although there have been no further infections, the mother stresses that her daughter seems to have a greater number of colds than her classmates and "has not seemed as healthy as she should be." However, the daughter's chart does not reflect an unusual number of office visits or calls. The mother also notes that the child's day-care center is next to "some kind of machine shop" where a chemical odor has been noticed recently. Several of the children and one of the teachers have complained of eye and throat irritation in association with the odor.

The mother, who is 33 years old, then reveals that she may be pregnant and she has had mild nausea for 1 week. It has been 8 weeks since her last menstrual period. Both parents are concerned about the possibility that the TCE in the drinking water might have affected the fetus. Although this pregnancy was planned, they might consider terminating the pregnancy if the baby was likely to be "damaged." They are also concerned that the entire family might suffer from cancer or other diseases in the future.

Before receiving bottled water, the family drank tap water when thirsty and made coffee with tap water. Tap water also was used for cooking and brushing their teeth, and is still used for bathing. They have never noticed discoloration or an off-taste to the tap water. They encourage their child to drink water instead of sodas during the summer and estimate the amount of water each of them consumes is 2 to 3 glasses a day.

You schedule each parent and the child for an individual office visit.

Pretest

(a) What would you include in the mother's and daughter's problem list?

(b) What additional information would you seek before seeing the family again?

(c) What reassurances might you provide at the end of this initial visit?

Answers to the Pretest can be found on page 19.

Exposure Pathways

- **The odor threshold of TCE is 20 to 80 ppm, which may not provide adequate warning of toxic levels.**
- **The most common sources of nonoccupational exposure to TCE are ambient air and drinking water.**

Trichloroethylene or TCE ($Cl_2C=CHCl$) is a clear, colorless, nonflammable liquid possessing a sweet, fruity odor characteristic of chloroform. The odor threshold is approximately 20 to 80 parts per million (ppm). For some workers, TCE's odor may not be detectable at concentrations near the permissible workplace exposure limit of 50 ppm (as determined by an 8-hour time-weighted average), and so may not provide adequate warning of its presence.

The official chemical name of trichloroethylene is trichloroethene. Other synonyms include TCE, TRI, acetylene trichloride, and ethylene trichloride. Trade names for this industrial solvent include Benzinol, Circosolve, Flock Flip, Narcogen, Perm-A-Chlor, Tri-clene, and Vestrol.*

TCE does not occur naturally; therefore, its presence indicates manufacture, use, or storage. Eighty percent of TCE is used for vapor degreasing of fabricated metal parts in the automotive and metal industries. Consumer products that contain TCE include typewriter correction fluids, paint removers/strippers, cosmetics, adhesives, spot removers, and cleaning fluids for rugs. Prior to its ban for certain applications in 1977, TCE was also used as a general (mostly obstetrical) anesthetic, analgesic, grain fumigant, disinfectant, pet food additive, and extractant of spices in foods and caffeine in coffee.

Occupational exposures may occur in chemical industries that manufacture polyvinyl chloride, pentachloroethane, and other polychlorinated aliphatic hydrocarbons, flame retardant chemicals, and insecticides. Other potential exposures occur in manufacturing processes of disinfectants, pharmaceuticals, dyes, perfumes, and soaps. Mechanics, oil processors, printers, resin workers, rubber cementers, shoe makers, textile and fabric cleaners, tobacco denicotinizers, varnish workers, and dry cleaners also have increased likelihood of TCE exposure, although most dry cleaners now use tetrachloroethylene (perchloroethylene) or 1,1,1-trichloroethane.

In the workplace, TCE is seldom present as a pure substance. Industrial grade TCE contains small amounts of stabilizers in the form of antioxidants or acid receptors; total chemical impurities usually do not exceed 0.1% by weight. Decomposition of TCE into dichloroacetylene (a neurotoxic compound) and phosgene

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

(a serious pulmonary irritant) occurs in the presence of alkali at temperatures above 60°C for the unstabilized compound and above 130°C for the stabilized compound.

Because of its widespread use, TCE has become a common environmental contaminant. Contamination results from evaporative losses during use; discharge to surface waters and groundwater by industry, commerce, and individual consumers; leaching from hazardous waste landfills into groundwater; and from the incidental addition of TCE during food production.

In the atmosphere, TCE is destroyed by photooxidation, with a half-life of less than 7 days. This relatively short half-life significantly limits the transport of TCE in air; however, the continual volatilization of TCE from emission sources or contaminated surface waters ensures its persistence in air. Examination of arctic air between 1982 and 1983 demonstrated mean TCE levels of 8 to 9 parts per trillion (ppt). This compares to mean concentrations of 30 ppt TCE in rural or remote areas, 460 ppt in urban and suburban areas, and up to 1200 ppt in areas nearest emission sources. Surveys have detected TCE in at least 460 of 1177 hazardous waste sites on the U.S. Environmental Protection Agency's (EPA) National Priorities List, with a maximum level of 12,300 ppt TCE in the ambient air at one New Jersey site.

TCE in drinking water is a result of its rapid leaching from landfills and its discharge from industrial wastewaters. TCE volatilizes quickly from water depending on temperature, water movement, and aeration. The biodegradation of TCE under anaerobic conditions is slow, making TCE relatively persistent in subsurface waters. An EPA groundwater survey detected TCE in approximately 10% of the wells tested. TCE is estimated to be in 34% of the nation's drinking water supplies.

Because of TCE's volatility, household activities such as bathing, laundering, and cooking with contaminated water may produce TCE air concentrations above normal ambient levels. Both natural and processed foods may contain TCE because of direct uptake through the environment, contamination of water used in food processing, and contamination by solvents used in cleaning food processing equipment. Most processed foods examined contain levels of a few parts per billion. Studies indicate that TCE does not bioaccumulate in the food chain.

Challenge

(1) What are the possible sources of exposure to trichloroethylene for the family described in the case study?

_____

_____

_____

Who's at Risk

- **Workers in metal fabricating and cleaning operations have the greatest likelihood of exposure to high concentrations of TCE.**
- **Because TCE inhalation can cause euphoria, deliberate abuse may occur.**
- **Ingestion of alcohol may potentiate the CNS depressant effects of TCE.**
- **A small subset of the population may be predisposed to developing ventricular fibrillation or asystole after exposure to high concentrations of TCE.**

Most significant exposures to TCE occur in the workplace. The National Institute for Occupational Safety and Health (NIOSH) has estimated that 3.5 million workers in the United States are exposed to TCE, with the majority of high exposures ascribed to metal degreasing operations. Sudden death has occurred in apparently healthy workers exposed to concentrations exceeding current legal workplace standards and in solvent abusers deliberately sniffing typewriter correction fluid from plastic bags or in enclosed spaces. Some of these deaths were due to asphyxia, whereas others were attributed to either ventricular fibrillation or asystole. Although no human studies have directly assessed potential dysrhythmogenic effects of TCE, there is no evidence that persons exposed to TCE at background environmental concentrations or at allowable workplace levels are at increased risk of developing cardiac dysrhythmias.

Until 1977, when certain uses were banned, TCE was employed as an inexpensive, nonflammable, and self-administered obstetrical anesthetic (Tri-lene*). It was discovered that alkali in rebreathing systems could lead to the production of dichloroacetylene, which produced cranial nerve injuries. Workers in environments containing this TCE-decomposition product also could be at risk of developing trigeminal, optic, or facial nerve effects.

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Alcohol potentiates TCE's effects on the central nervous system. Concurrent alcohol consumption and exposure to TCE can result in "degreaser's flush," a temporary redness and itching of the back, neck, and face. Theoretically, liver dysfunction or disulfiram (Antabuse[R]*) treatment could reduce the metabolism of TCE and thus increase its CNS depressant effects.

TCE is one of the volatile organic contaminants most frequently found in groundwater. The possibility of an association between ingested TCE and long-term effects, including malignancies, has been raised, but scientific evidence proving that these effects are due to TCE exposure is lacking. To gather information on the health effects of ingesting TCE-contaminated water, ATSDR, in cooperation with the States, has established a national registry. This registry is discussed in Sources of Information, page 20.

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(2) Which members of the family described in the case study are at increased risk for adverse effects from TCE? Explain.

Biologic Fate

- **Pulmonary and gastrointestinal absorption of TCE is rapid; dermal absorption is relatively slow.**

- **TCE metabolism occurs mainly in the liver.**

- **Species differences in TCE metabolism require that caution be used in extrapolating adverse effects to humans.**

At 100 to 200 ppm TCE, the lungs of human volunteers absorbed approximately 50% of an inhaled dose during the first 30 minutes of exposure. Case reports of human poisoning after ingestion of TCE indicate that gastrointestinal absorption is also substantial. Dermal TCE absorption in humans may add to the body burden, but toxicity from this source alone is unlikely. In contrast to direct contact of the skin with liquid TCE, absorption of its vapor through the skin is negligible.

Once absorbed, TCE is rapidly cleared from the blood. Due to its lipid solubility, TCE accumulation occurs in organs containing high levels of adipose tissue. Data from animal studies indicate that body fat, adrenal glands, ovaries, and cellular components of the blood accumulate the greatest portion of absorbed TCE. TCE rapidly crosses the placenta in both humans and animals, and can accumulate in the fetus.

In humans, TCE is metabolized primarily in the liver by the mixed function oxidase system that probably converts TCE to an oxide (epoxide). Subsequently, this reactive intermediate may rearrange to trichloroacetaldehyde and then chloral hydrate, the latter forming the trichloroethanol and trichloroacetic acid metabolites excreted in the urine after TCE exposure. At 54 to 140 ppm TCE, human volunteers metabolized approximately 90% of an inhaled dose. No studies have provided evidence of saturation of TCE metabolism in humans, at least for inhaled concentrations to 300 ppm.

A relatively small amount of absorbed TCE is exhaled unchanged; most of an absorbed dose is metabolized and excreted in the urine. After exposure to air concentrations between 100 and 200 ppm, approximately 30% to 50% of an absorbed dose appears in urine as trichloroethanol, and about 10% to 30% appears as trichloroacetic acid. The time between TCE inhalation and urinary excretion of trichloroethanol is relatively short (biologic half-life approximately 10 hours) compared with the urinary excretion of trichloroacetic acid (biologic half-life approximately 52 hours). Trichloroacetic acid is theoretically detectable in urine for at least a week after TCE exposure.

(3) Additional information for the case study: On the next visit to your office, the mother states that some families in their neighborhood are being seen by another practitioner, who has sent specimens to a laboratory for measurement of indicators of trichloroethylene exposure.

What biologic indicators of TCE exposure are likely being measured?

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(4) If biologic measurements are performed, what considerations should be taken into account to properly interpret the results?

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Physiologic Effects

Studies in humans show that TCE produces CNS effects, mucous membrane, skin, and gastrointestinal irritation, decreased appetite, and headache. However, these results are inconsistent with those of better designed studies. Hepatotoxicity has been associated primarily with intentional TCE inhalation abuse. Renal failure has been reported in concert with confirmed hepatic damage. Cardiac dysrhythmias due to TCE exposure may be induced in susceptible persons.

Central Nervous System Effects

TCE-induced CNS symptoms depend on both concentration and exposure duration. In one study of human volunteers, exposure to TCE air levels of 27 ppm for 4 hours caused drowsiness and mucous membrane irritation, and at 81 ppm, headaches. In another study, drowsiness, lethargy, and nausea were noted within 5 minutes at anesthetic concentrations of 2000 ppm. TCE presumably causes anesthesia by affecting cell membranes and

❑ **CNS depression is the most prominent effect of acute TCE exposure.**

- **Chronic occupational TCE exposure has been associated with neurologic abnormalities.**

altering neuronal transmission. Symptoms due to short-term exposures typically resolve within a few hours of exposure.

In a study of 50 workers employed from 1 month to 15 years in various industrial cleaning and degreasing operations using TCE, complaints due to chronic exposure included decreased appetite, sleep disturbances, ataxia, vertigo, headache, short-term memory loss, and fewer word associations. Greater frequency of symptoms were noted in workers exposed to higher (85 ppm) than lower (14 ppm) mean TCE concentrations.

In the brains of animals chronically exposed to high concentrations of TCE (1000 ppm to 3000 ppm), histologic changes have been demonstrated, but these changes do not correlate with behavioral abnormalities detected in animals or humans. Persons who have deliberately abused volatile chlorocarbon solvents have developed cerebellar damage and ataxia. Electrophysiologic studies in humans have not detected significant abnormalities of peripheral nerve conduction.

Cardiovascular Effects

- **Death due to cardiac dysrythmia in TCE-exposed workers has been associated with high doses in conjunction with vigorous physical activity.**

Mortality studies of TCE-exposed workers do not indicate an increased risk of cardiovascular death. A few susceptible persons who are exposed to near-anesthetic levels during vigorous activity may have increased risk of cardiac dysrythmia. However, there is no evidence that exposure at high TCE levels causes a predisposition to cardiac toxicity at lower levels. When TCE was administered as an anesthetic agent, serious ventricular dysrhythmias and cardiac arrests were rare and were nearly always associated with hypoxia. Significant ventricular ectopy would not be expected from TCE exposure at background environmental levels or those currently allowed in the workplace.

Gastrointestinal and Renal Effects

- **Case reports associate liver damage with inhalation of high doses of TCE.**
- **Human nephrotoxicity due to TCE exposure is rare and generally occurs in persons with TCE-induced hepatic damage.**

When swallowed, TCE causes gastrointestinal irritation, with possible inflammation of the GI tract manifested as nausea, vomiting, diarrhea, and abdominal pain. Hepatotoxicity has been associated primarily with intentional TCE inhalation abuse. In these cases, hepatic histologic examination has revealed centrilobular necrosis with fatty infiltration. Chronic TCE exposures at concentrations currently permissible in the workplace or at those expected in ambient air are not likely to cause liver damage.

TCE-induced renal failure in humans has been reported, albeit infrequently, and usually in concert with confirmed hepatic damage. One case involved a long-time metal degreaser who developed acute tubular necrosis (confirmed by biopsy), which led to renal failure. Another case involved a worker exposed to 99.5% TCE for 8 hours; he developed allergic interstitial nephritis with secondary tubular necrosis. Animals demonstrate little nephrotoxicity after single, high-dose exposures.

Reproductive and Developmental Effects

- **Limited studies in workers have not detected significant reproductive or developmental abnormalities due to TCE exposure.**

No increased incidence of congenital malformations has been detected in babies born to mothers occupationally exposed to TCE. A small cross-sectional study of degreasing workers showed no effect of TCE exposure on male germ cells. Data from animal studies reveal no adverse effects on reproductive system histology, fertility, or other reproductive performance parameters.

TCE crosses the placenta in animals and has been found in human newborns after maternal TCE anesthesia during childbirth. Human developmental effects were attributed to the ingestion of TCE-contaminated water in one study, but the significance of this finding is questionable because of mixed chemical exposures and methodologic inadequacies of the study. In animals, abnormalities (decreased fetal body weight and ossification anomalies) have been reported infrequently.

Carcinogenic Effects

- **The few epidemiologic studies of TCE-exposed persons to determine cancer risk are inconclusive.**

Inhalation or oral exposure to high doses of TCE produces liver and lung tumors in mice, and renal adenocarcinomas, testicular tumors, and possibly leukemia in rats. The relevance of the liver tumor data obtained from the mice used in these studies is controversial because the species used tends to form spontaneous liver tumors. The presence of TCE stabilizers, such as epichlorohydrin, may also confound some of these results. These studies indicate that mice are more susceptible than rats to TCE carcinogenicity.

Most early epidemiologic studies of workplace exposures to TCE did not demonstrate a significant increase in the incidence of cancer. A recent follow-up study of workers, however, found excesses of bladder cancer and lymphomas. The significance of this study has yet to be confirmed. Some inconsistencies between results of animal and human studies may be due to

metabolic saturation and formation of reactive intermediates that occur in animals exposed to high TCE levels but not in humans after low-level exposure.

EPA considers the weight of evidence sufficient to conclude that TCE is carcinogenic in animals and a probable human carcinogen. However, the animal studies do not meet the National Toxicology Program (NTP) guidelines (i.e., positive carcinogenicity in multiple species of both sexes); therefore, TCE is not listed as a carcinogen in NTP's most recent report.

Other Effects

- **TCE is a mild respiratory tract irritant and may produce contact dermatitis.**
- **Evidence does not show that TCE adversely affects the human immune system.**

TCE produces minimal irritation of the respiratory tract except at concentrations exceeding current workplace standards. Use of TCE in anesthetic concentrations did not damage the pulmonary system. TCE is not a sensitizing agent, and bronchospasm is unlikely to occur except in highly susceptible persons after exposure to high concentrations. Rarely are patch tests positive for allergic reaction.

Like other organic solvents, TCE may produce contact dermatitis, rashes, and burns. The defatting dermatitis resulting from prolonged contact may reduce resistance to skin infections. An irritant reaction resembling an exfoliative dermatitis or scarlatiniform reaction may occur from dermal contact with contaminated clothing.

A syndrome called degreaser's flush has been associated with the interaction of ingested ethanol and inhaled TCE. Typically, erythema resulting from vasodilation develops around the face, back, and shoulders within 30 minutes and resolves within an hour of appearance.

No deleterious effects on the immune system have been noted in persons exposed to TCE through environmental sources. Immunologic studies in animals are inconclusive.

(5) Additional information for the case study: The father says that he has felt increasingly tired and easily fatigued for the past few months. Results of his physical examination are entirely within normal limits. What tests, if any, would you order?

(6) Additional information: The mother's obstetrician calls 1 month later. Examination, including sonogram, is normal for her stage of pregnancy. The obstetrician asks you about the potential fetotoxicity of TCE and whether a more invasive evaluation (amniocentesis, chorionic villus biopsy) is indicated. What is your response?

Clinical Evaluation

History and Physical Examination

No unique pattern of symptoms characterizes TCE-induced illness. An occupational history should be routinely obtained and should include items such as company name and location, job title, description of chemical processes encountered, known toxic agents used, workplace investigations, and coworker complaints. An environmental history should also be obtained, including location and duration of residence, proximity to industry, diet, daily activities, type of water supply, and use of consumer products that contain TCE.

The patient's complaints should be identified in terms of onset, duration, and intensity. Complaints should be investigated by focusing first on organ systems that are likely to be affected by exposure to TCE (CNS, hepatic, integumentary), and then on systems unlikely to be affected (respiratory, cardiovascular, renal, gastrointestinal, endocrine, skeletal). Patients should receive a complete neurologic examination, including a mental status exam and evaluation of the cranial nerves to detect either

- **TCE exposure produces no unique clinical clues.**

peripheral or central nervous system involvement. Cranial neuropathies in patients with a history of TCE exposure, while uncommon, suggest exposure to dichloroacetylene. Presence or absence of an irregular pulse or abnormal cardiac auscultation should be noted. The patient's abdomen should be palpated for hepatomegaly and right upper quadrant tenderness.

Signs and Symptoms

Acute Exposure

Respiratory depression can result from acute, high-dose TCE exposure.

With inhalation of high concentrations, TCE causes initial CNS excitation followed by CNS depression. Depending on the duration and intensity of exposure, symptoms may be drowsiness, dizziness, visual disturbances, lightheadedness, fatigue, headache, lethargy, confusion, ataxia, and stupor. Coma and respiratory depression may occur with prolonged, high-level exposure (i.e., above 2000 ppm). Serious ventricular dysrhythmias can develop up to 24 hours after large TCE ingestions.

After any type of acute exposure, the clinician should carefully assess the adequacy of ventilation (respiratory depression is the most common serious sequelae of acute TCE exposure). Because of possible dysrhythmias, patients with preexisting cardiovascular disease should be monitored by continuous ECG and frequent evaluation of vital signs. Since hepatic injury may occur, liver function tests should be performed.

Chronic Exposure

At permissible workplace levels, CNS symptoms of TCE exposure are usually nonspecific and transient.

Reported neurologic effects associated with chronic workplace exposure to TCE have included nonspecific symptoms such as headache, ataxia, decreased appetite, sleep disturbances, fatigue, weakness, dizziness, memory loss, emotional instability, impaired judgment. However, study design defects (e.g., exposure data that does not allow for differentiation of acute and chronic effects, failure to analyze confounding variables, lack of controls, and observer bias) limit the conclusion that chronic TCE exposure may cause these effects.

Although CNS symptoms may disappear within several weeks after cessation of exposure, some health effects may persist in persons who have been exposed to TCE for long periods. Persistent neurologic symptoms should also prompt a search for exposure to other potential neurotoxins, such as carbon disulfide, methanol, or n-hexane; drugs of abuse, including alcohol; or psychiatric disorders.

Laboratory Tests

Direct Biologic Indicators

Data are limited for interpreting TCE levels in plasma. Detectable plasma levels of TCE in persons without occupational exposure are approximately 0.01 to 0.13 micrograms per deciliter (µg/dL). Although TCE disappears rapidly from the blood, metabolites (e.g., trichloroacetic acid) may persist in the blood for several weeks and in urine up to 3 weeks after heavy exposure. The presence of TCE metabolites should be interpreted with caution because medications (chloral hydrate, disulfiram) and other chlorinated hydrocarbons (1,1,1-trichloroethane, tetrachloroethylene) are also metabolized to trichloroacetic acid and excreted in the urine. TCE may appear on abdominal X rays as a radiopaque material after ingestion.

- **TCE may be measured in the breath and urine up to 16 hours after exposure; metabolites may persist for a week or more.**
- **Urinary metabolites are trichloroethanol and trichloroacetic acid.**

Indirect Biologic Indicators

Biochemical abnormalities are uncommon after acute TCE exposures. Rarely have elevations of serum hepatic transaminases (SGOT or AST, SGPT or ALT), bilirubin, and creatinine resulted from acute TCE exposure; nevertheless, liver function and serum creatinine tests should be performed to establish baselines. Electrocardiogram and continuous cardiac monitoring should be considered for heavily exposed persons. Ingestion of large amounts of TCE causing profuse diarrhea may produce an electrolyte imbalance. Because the trigeminal, optic, and facial nerves may be impaired by exposure to dichloroacetylene, changes in the visual fields and trigeminal nerve potentials may be noted.

- **Liver function tests, a serum creatinine test, and continuous cardiac monitoring should be considered for persons acutely exposed to TCE.**

Challenge

(7) Additional information for the case study: You evaluate the 4-year-old child. Review of her history reveals three to four episodes of otitis media in each of the last 3 years, which were treated with ampicillin. The child was placed on continuous prophylactic antibiotics during the last two cold seasons. Last year, the child developed additional infections despite the antibiotic regimen, and you referred her to an otolaryngologist, who performed a myringotomy and tympanostomy without incident. The mother estimates the child has had four episodes of coryza or mild influenza last year, with about 7 days of illness that merited staying home from day care.

Does this pattern reflect compromise of the child's immune system?

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_____

(8) The mother asks about immune system tests. A health care practitioner evaluating other families has performed such tests. Is the assessment of immunocompetence appropriate in this case?

_____

_____

Treatment and Management

Acute Exposure

In the case of dermal contact with liquid TCE, contaminated clothes should be removed and the affected areas washed with copious amounts of soap and water. Direct eye splashes require irrigation for at least 15 minutes. Corneal epithelium damage usually resolves spontaneously after irrigation.

- **Removal from the source and supportive care is the recommended treatment for acute TCE exposure.**

Patients should be removed from the contaminated environment as soon as possible; begin artificial ventilation, if needed. Those with altered mental status or apparent respiratory insufficiency should receive supplemental oxygen. If the patient's pulse is absent, cardiopulmonary resuscitation should be initiated.

Gut decontamination (emesis, lavage, saline cathartic) is recommended if it can be initiated within 2 to 3 hours after ingestion of more than a swallow of TCE. However, the effects of these measures have not been clinically evaluated. If emesis is considered, administer the emetic only to patients who are fully conscious and have an intact gag reflex. Activated charcoal has not been proven to absorb TCE, but in general, effectively decreases absorption of most ingested toxic agents. No data are available on the ability of hemodialysis or hemoperfusion to increase TCE elimination. There are no specific antidotes.

Patients with serious TCE toxicity should be monitored for the possible development of dysrhythmias. When diarrhea is present, monitor for the development of electrolyte abnormalities and screen for the possible development of hepatorenal dysfunction. Sequelae are unusual with acute exposures.

Chronic Exposure

There is no known treatment for chronic exposure to TCE. Potentially involved organ systems should be independently evaluated and supportive measures initiated.

- **Symptomatic treatment is recommended for chronic TCE exposure.**

Standards and Regulations

Workplace

Air

OSHA's current PEL is 50 ppm.

In 1989, the Occupational Safety and Health Administration (OSHA) lowered the permissible exposure limit (PEL) from a time-weighted average (TWA) of 100 ppm to 50 ppm, with 200 ppm TCE as a short-term exposure limit (STEL). The TWA concentration for a normal 8-hour workday and 40-hour workweek is set at a level at which nearly all workers may be repeatedly exposed without adverse effects. The STEL for TCE is a concentration at which workers can be exposed continuously for a short period of time (usually 15 minutes) without suffering irritation, chronic irreversible tissue damage, or narcosis. NIOSH recommends a 10-hour TWA of 25 ppm. Table 1 summarizes current standards and regulations for TCE exposure.

Table 1. Standards and regulations for trichloroethylene

Agency*	Focus	Level	Comments
ACGIH	Air -Workplace	50 ppm	Advisory; TWA†
NIOSH	Air -Workplace	25 ppm	Advisory; TWA†
OSHA	Air -Workplace	50 ppm	Regulation; PEL§ over 8-hour workday
		200 ppm	Regulation; STEL¶
EPA	Air-Environment	N/A	Under review
	Drinking Water	5 ppb	Regulation

* 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

† TWA (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.

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

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

Biologic exposure indices are recommended by the American Conference of Governmental Industrial Hygienists and may involve either direct or indirect measures of individual worker exposure. An end-exhaled air sample collected 16 hours after the last TCE exposure (i.e., prior to the next shift) should be 0.4 ppm or less. Free trichloroethanol in the blood may be measured, but a number of other compounds affect the level of trichloroethanol and must be considered as alternate explanations for elevated levels.

Alternatively, a concentration of 100 milligrams (mg) of trichloroacetic acid per liter (L) of urine at the end of the work week reflects the upper biologic limit for TCE exposure. Urinary trichloroacetic acid levels can be increased by the same compounds that affect blood trichloroethanol levels. Because of large individual variations, this urinary trichloroacetic acid level of 100 mg/L should be used only as a "warning" level or mean for a group of workers.

Environment

Environmental exposures to TCE are generally low and are decreasing since limitations have been imposed on its use as an anesthetic, solvent extractant, fumigant, and dry-cleaning agent. TCE has a short atmospheric half-life (less than 7 days) and does not accumulate in the food chain. The World Health Organization recommended drinking water limit is 30 µg TCE/L of water (30 ppb); EPA recommends a maximum contaminant level of 5 µg/L (5 ppb) in drinking water. Based on the available data, no known human health effects are associated with exposures to environmental levels of TCE, but more comprehensive information is necessary for a final assessment.

Challenge

(9) TCE has been identified as the irritant at the day-care center. The mother described in the case study is concerned and wishes to take action to get the level reduced. What can you recommend to her?

Suggested Reading List

General

Fan AM. Trichloroethylene: water contamination and health risk assessment. Rev Environ Contam Toxicol 1988;101:55-92.

Feldman RG, White RF, Currie JN, Travers PH, Lessell S. Long-term follow-up after single toxic exposure to trichloroethylene. Am J Ind Med 1985;8:119-26.

International Agency for Research on Cancer: IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans, Suppl 7. Trichloroethylene. Lyons, France: World Health Organization, 1987.

International Programme on Chemical Safety: Environmental Health Criteria 50 Trichloroethylene, Geneva: World Health Organization, 1985.

Kimbrough RD, Mitchell FL, Houk VN. Trichloroethylene: an update. J Toxicol Environ Health 1985;15: 369-83.

Shindell S, Ulrich S. A cohort study of employees of a manufacturing plant using trichloroethylene. J Occup Med 1985;27:577-9.

Smith GF. Trichloroethylene: a review. Br J Ind Med 1966;23:249-62.

Tola S, Vilhunen R, Jarvinen E, Korkala ML. A cohort study on workers exposed to trichloroethylene. J Occup Med 1980;22:737-40.

Specific Health Effects

Adams RM. Degreaser's flush. West J Med 1976;125:487.

Forkert PG, Sylvestre PL, Poland JS. Lung injury induced by trichloroethylene. Toxicology 1985; 35: 143-60.

King GS, Smialek JE, Troutmen WG. Sudden death in adolescents resulting from the inhalation of typewriter correction fluid. JAMA 1985;253:1604-6.

Lawrence WH, Partyka EK. Chronic dysphagia and trigeminal anesthesia after trichloroethylene exposure. Ann Intern Med 1981;95:710.

Related Government Publications

Agency for Toxic Substances and Disease Registry. Toxicological profile for trichloroethylene. Atlanta: US Department of Health and Human Services, Public Health Service, 1989. NTIS report no. PB/90/ 127523/AS.

Environmental Protection Agency. Health assessment document for trichloroethylene. Final report. Washington, DC: EPA, 1985. NTIS report no. PB/85-249696.

Environmental Protection Agency. Addendum to the health assessment document for trichloroethylene: update carcinogenicity assessment for trichloroethylene. Review draft. June 1987. Report No. EPA/ 600/8-82/006FA.

Answers to Pretest and Challenge Questions

Pretest

Pretest is found on page 1.

(a) The mother's problem list includes pregnancy and anxiety; and the child's, frequent otitis media (status post myringotomy and tympanostomy tube placement) and frequent upper respiratory infections.

(b) You will need information on TCE toxicity, including reproductive and developmental effects; information on TCE contamination of the family's drinking water, including duration of contamination; copies of information provided to the family by the municipal water company; and responses, if any, from local and state health agencies.

(c) None of the symptoms described in the case indicates serious illness. However, you should reassure the family that you will perform complete physical examinations with appropriate testing at the next visit. In response to concern about the child's infections, you should indicate that you will collect information about possible TCE effects on the immune system. Explain to the parents that tests of immune function are often difficult to interpret and may not be appropriate. You may indicate that you will consult sources of information on TCE's effects on pregnancy. It is important to maintain a balance between reassurance that the unborn child is probably not affected by the water contamination and concern for the possible risk to the fetus. Reassurance should not, however, appear to trivialize the family's fears. It would also be appropriate to discuss that no evaluation, however thorough, can totally exclude the possibility that a person may develop an illness, including cancer.

Challenge

Challenge questions begin on page 4.

(1) Possible sources of the family's TCE exposure include home drinking water (dermal and inhalation exposure during bathing, and ingestion), father's workplace (inhalation), and the daughter's day-care center (inhalation). Minor sources might be certain foods such as margarine (ingestion) and use of TCE-containing consumer products such as correction fluid, spot removers, etc. (inhalation).

(2) From the information about the family thus far, none of them fits the profile of a person at increased risk from the effects of TCE exposure. That is, there is no indication that any family member has liver dysfunction or cardiac disorders, abuses TCE, or consumes large amounts of alcohol.

(3) The most convenient biologic indicators of TCE exposure are the urinary metabolites, trichloroethanol and trichloroacetic acid. These metabolites are not specific to TCE, however, since they are also metabolites of tetrachloroethylene (perchloroethylene) and 1,1,1-trichloroethane (methyl chloroform) and certain medications. TCE itself can be measured directly in blood or exhaled air, but because of the difficulty of obtaining samples, such measurements are not indicated here.

(4) To properly interpret any of the tests mentioned in (3), a knowledge of the time-lapse between exposure and collection is necessary. To prevent contamination or sample loss (evaporation, adsorption), the proper collection, handling, storage, and transportation procedures must be followed. It is unlikely that any member of this family would have levels of TCE or its metabolites significantly above background levels. Furthermore, there are no appropriate reference values currently available for a health risk assessment.

(5) No further studies are indicated for TCE exposure. A workup for fatigue may indicate additional tests.

(6) Based on limited evidence from animal studies, researchers believe teratogenicity does not occur at environmental TCE levels. Invasive procedures are not justified on the basis of the drinking water contamination.

(7) No, a recent survey of infections in children under 3 years of age over a September to March period found an average of 2.5 total infections and more than one episode of otitis media per child (1.4 episodes per child for those in day care). Over 3% of the children in day care were hospitalized for tympanostomies. (Reference: Bell DM, Gleiber DW, Mercer AA, et al. Illness associated with child day care: a study of incidence and cost. Am J Public Health 1989;79:479-84.) The child described in the case study appears to have an above-average rate of infections, but they are not frequent enough to suggest immunologic impairment.

(8) No, immunocompetence tests are not appropriate because no evidence of immune function abnormalities has been found in similar situations. Nevertheless, physicians may be asked to explain further why they are not performing the tests on their patients. Two references that may be of value are (1) Kahn E, Letz G. Clinical ecology:environmental medicine or unsubstantiated theory? Ann Intern Med 1989; 2:104-6; and (2) American College of Physicians. Clinical ecology. Ann Intern Med 1989;2:168-78.

If it had been indicated, laboratory evaluation of immunologic host-defense defects would consist of three phases. The preliminary screening is a complete blood count with differential smear and quantitative immunoglobulin levels. These tests, together with history and physical examination, will identify more than 95% of patients with primary immunodeficiencies. The second phase of testing consists of readily available studies including B-cell function (such as antibodies, response to immunization), T-cell function (skin tests, contact sensitization), and complement levels. The first two phases combined will detect most immunodeficiencies amenable to conventional treatment with gamma globulin or plasma. The third phase (in-depth investigation) consists of testing induction of B lymphocyte differentiation in vitro, stimulated by pokeweed mitogen and histologic and immunofluorescent examination of biopsy specimens; T-cell surface markers; assays of T-cell helper or killer cell functions; and functional assays using appropriate target cells. It is inappropriate to perform these latter tests on environmentally exposed patients except for epidemiologic research.

Primary immunodeficiency is suspected in an infant who has repeated upper respiratory tract or other infections. It is also suspected if repeated infection occurs in a child who has had little exposure to infectious agents, or any child with unusual infections, incomplete clearing of infections, growth failure, hepatosplenomegaly, or features associated with specific immunodeficiency disorders, such as ataxia or telangiectasia. The child described in the case study has none of these indications.

(9) EPA has not issued an emission standard for TCE. Assuming discussions with the owner or operator of the shop adjacent to the day-care center have not been effective in reducing the level of ambient TCE, the community's air pollution control center should be notified. States may allow this control under the jurisdiction of local air pollution control districts, county health departments, or other local agencies. The agency responsible for enforcement of air standards should be contacted to investigate possible release of TCE onto the day-care center property.

Sources of Information

In addition to other resources, ATSDR has created a National Exposure Registry for trichloroethylene. This registry is the first in a series of registries mandated by the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA). ATSDR, in cooperation with the States, will establish and maintain national registries of (1) persons exposed to substances and (2) persons with serious illness

or diseases possibly due to exposure. The registries will collect information on the effects of low-level exposures of long duration (the exposures typically found in populations surrounding hazardous waste sites) and the health outcomes for populations receiving a one-time, high-level environmental exposure (such as those experienced at chemical spill sites). The registries will facilitate the identification and subsequent tracking of persons exposed to a defined substance at selected sites and will coordinate the clinical and research activities involving the registrants. For further information on the trichloroethylene registry, please contact ATSDR in Atlanta, Georgia.

More information on the adverse effects of trichloroethylene and the treatment and management of trichloroethylene-exposed persons can be obtained from ATSDR, your state and local health departments, and university medical centers. *Case Studies in Environmental Medicine: Trichloroethylene 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) 639-6204.

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 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 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.

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) 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: TRICHLOROETHYLENE

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

1. Acute TCE exposure can adversely affect all of the following except
   a. CNS
   b. skin
   c. pancreas
   d. mucous membranes
   e. joints
2. Chronic exposure to TCE may
   a. cause headaches or drowsiness
   b. mildly alter liver function
   c. cause short-term memory deficits
   d. cause Alzheimer's disease
   e. result in Gilbert's syndrome
3. Laboratory tests to confirm TCE exposure include
   a. blood analysis for trichloroethanol
   b. breath analysis for trichloroacetic acid
   c. urinary creatine
   d. cardiac isoenzymes
   e. urinary trichloroacetic acid
4. Common clinical effects associated with acute exposure to pure TCE at concentrations greater than 2000 ppm include
   a. trigeminal neuralgia
   b. peripheral neuropathy
   c. CNS depression
   d. nausea
   e. upper respiratory tract and eye irritation
5. Drinking water contaminated with low levels of TCE has been conclusively associated with
   a. trigeminal neuralgia
   b. cardiac ventricular dysrhythmias
   c. hepatorenal syndrome
   d. no specific pathology
   e. cleft palate in children born to exposed pregnant women
6. Cardiac toxicity due to TCE exposure
   a. is a frequent cause of death among dry-cleaning workers
   b. has not caused increased mortality among metal degreasers
   c. is caused by the metabolism of TCE to carbon monoxide
   d. may lead to dysrhythmias
   e. may be due to arteriosclerosis
7. Treatment for acute inhalation of TCE may include
   a. symptomatic support
   b. inducing emesis
   c. hemodialysis
   d. oxygen
   e. milk of magnesia
8. Likelihood of TCE exposure exists for
   a. accountants
   b. automobile parts manufacturers
   c. judges
   d. electronic workers
   e. race car drivers

CASE STUDIES IN ENVIRONMENTAL MEDICINE: TRICHLOROETHYLENE

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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4. a b c d e
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6. a b c d e
7. a b c d e
8. a b c d e

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   Yes No Undecided

2. Was the amount of detail appropriate?

   Too technical Just right Not technical enough

3. As a result of reading this issue, will you now ask patients more questions regarding possible environmental exposures?

   Yes No Undecided Not applicable

4. Would you recommend this issue to your colleagues?

   Yes No Undecided

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- ☐ methylene chloride
- ☐ nitrates/nitrites
- ☐ phenols
- ☐ polyaromatic hydrocarbons (PAHs)
- ☐ polychlorinated biphenyls (PCBs)
- ☐ radon
- ☐ tetrachloroethylene
- ☐ 1,1,1-trichloroethane
- ☐ trichloroethylene
- ☐ toluene
- ☐ vinyl chloride
- ☐ Exposure History
- ☐ Risk Communication
- ☐ Skin Diseases

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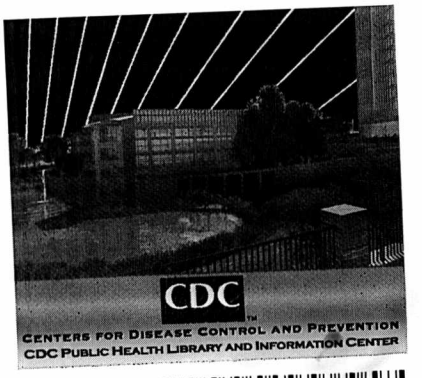

The state of knowledge regarding the treatment of patients potentially exposed to hazardous substances in the environment is constantly evolving and is often uncertain. In this monograph, the Agency for Toxic Substances and Disease Registry (ATSDR) has made diligent effort to ensure the accuracy and 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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