AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY
Case Studies in Environmental Medicine

Tetrachloroethylene Toxicity

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Background

About this and other ATSDR Case Studies in Environmental Medicine	This educational case study document is one in a series of self-instructional modules designed to increase the primary health care provider's knowledge of hazardous substances in the environment and to promote medical practices that aid in the prevention, evaluation and care of potentially exposed patients. The complete series of ATSDR Case Studies in Environmental Medicine is located on the ATSDR Web site at URL: **https://www.atsdr.cdc.gov/csem/csem.html** In addition, the downloadable PDF version **https://www.atsdr.cdc.gov/csem/Tetrachloroethylene_Toxicity/docs/TetrachloroethyleneToxicity-H.pdf** of this educational series and other environmental medicine materials provides content in an electronic, printable format, especially for those who may lack adequate Internet service.
Acknowledgements	We gratefully acknowledge the work of the medical writers, editors, and reviewers in producing this educational resource. Contributors to this version of the "ATSDR Case Studies in Environmental Medicine: Lead Toxicity" manuscript are listed below. Please Note: Each content expert for this case study has indicated that there is no conflict of interest that would bias the case study content. **ATSDR Authors:** Dianyi Yu, M.D. **ATSDR Planners:** Germania Pinheiro, M.D., MSc, Ph.D; Brian Tencza, M.Ed; John Doyle, M.P.A.; Diana Cronin **Peer Reviewers:** Jessica Weiland, M.D.; Rae Benedict, Ph. D
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Course Overview

Course overview	This Case Study in Environmental Medicine (CSEM) provides an overview of tetrachloroethylene toxicity. Tetrachloroethylene is a chemical used in dry cleaning and other applications. Knowledge from this course will help health care providers diagnose and treat patients exposed to tetrachloroethylene. This online course will take about 150 minutes to complete. You may finish the entire CSEM in one session or complete each chapter separately. The course begins with a patient case study to help you assess your current knowledge about tetrachloroethylene toxicity. You can earn continuing education (CE) credits for the course by completing it online.

Course Learning objectives	After completing this course, you will be able to • Define tetrachloroethylene; • Describe uses of tetrachloroethylene; • Identify sources of tetrachloroethylene exposure; • Describe how people are exposed to tetrachloroethylene, • Identify populations with potentially high exposures to tetrachloroethylene; • Explain the major pathways of tetrachloroethylene metabolism in the body; • Describe the clinical effects associated with tetrachloroethylene exposure; • Describe what is included in the initial history of patients potentially exposed to tetrachloroethylene; • Describe what is included in the physical examination of patients potentially exposed to tetrachloroethylene; • Describe possible clinical symptoms in patients exposed to tetrachloroethylene; • Identify tests that can help diagnose tetrachloroethylene toxicity; • Describe treatment strategies for patients with tetrachloroethylene poisoning; • Identify existing standards and guidelines for tetrachloroethylene in the environment; • Identify existing standards and guidelines for tetrachloroethylene in the workplace; • Identify suitable self-care for patients exposed to tetrachloroethylene; • Identify clinical follow-up for patients exposed to tetrachloroethylene; • Describe how to counsel patients appropriately on how to avoid further exposure to tetrachloroethylene.
Key concepts	Key concepts in this course include 1. Tetrachloroethylene is used mainly as a solvent for dry cleaning and metal degreasing. 2. Like most chlorinated solvents, tetrachloroethylene can cause central nervous system depression. 3. Chronic exposure to tetrachloroethylene can adversely affect the neurological system, liver, and kidneys. 4. Tetrachloroethylene is considered a human carcinogen, based on limited evidence from studies in humans and sufficient evidence from studies in experimental animals. 5. Tetrachloroethylene toxicity has no antidote. 6. In December 2020, federal regulations will require dry cleaners in urban locations to eliminate the use of tetrachloroethylene.

CSEM overview	The goals of CSEM series are to • increase the primary care provider's knowledge of hazardous substances in the environment, and • help clinicians evaluate and treat potentially exposed patients. You can find the complete series of CSEMs online at http://www.atsdr.cdc.gov/csem/csem.html You can download and print PDFs of this educational series and other environmental medicine materials from the ATSDR website.

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Pre-course Knowledge Check

Introduction	This case study will help you assess your pre-course knowledge about tetrachloroethylene toxicity. Read the case presentation and answer the questions that follow.
Case presentation	A 37-year-old woman who is 4 months postpartum visits her physician's office with complaints of headache, increasing irritability, and difficulty concentrating. She says she has become impatient and short-tempered with her husband and new child and becomes angry about minor things. These feelings began about 1 month ago. She is most irritable in the evenings, when she also has a throbbing frontal headache. She has no psychiatric history. She has been having three drinks of alcohol a day since her marriage 4 years ago. However, she did not drink during the pregnancy and does not use other drugs or medications. She has 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 she returned 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 pesticide. Her husband feels fine and has not been ill. Her infant daughter's delivery was uneventful. The baby appears to be developing normally, but has been "very fussy" lately. The infant, whom the physician saw 5 weeks ago for otitis media, is still breast-feeding. One month ago, the patient returned to her job as a word processor. She works mornings and relaxes with her new hobby, silk screening, in the afternoons. 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 might lead to conflict with her supervisor. The patient had no history of headaches before she resumed her job and began her silk printing hobby.

Physical examination	**Vital signs:** Blood pressure: 125/85 mmHg; pulse: 68 beats/minute and regular; respirations: 14 breaths/minute; temperature: 98.6°F (37°C) **Head, ears, eyes, nose, and throat (HEENT); respiratory; cardiovascular; and abdominal examinations:** The physical examination reveals that the woman is slightly overweight. Her nail beds are pale. 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. She has no focal muscle tension or tenderness. Her liver is not enlarged, and examination of the abdomen is unremarkable. Respiratory and cardiovascular examination results are normal with no crucial findings. **Skin:** She has no skin rashes, lesions, or stigmata of liver disease. **Neurology**: The patient's neurological examination results are within normal limits. Her recent and distant memory are intact. Proverb interpretation and mini-mental state examination results are normal. Sensory and motor functions are normal, as are Romberg test results and gait. Deep tendon reflexes are normal and symmetrical.
Questions	1. What should be included in this patient's problem list? 2. What further information would assist in establishing a diagnosis? 3. What laboratory tests would a physician order for this patient? 4. On questioning, the patient explains that silk screening involves stretching a large piece of cloth across a support frame, masking it to create a pattern, then dying the unmasked areas. The cloth is cleaned before masking. The patient mentions that she started using a new fabric cleaner 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 container does not list the contents, how can the doctor determine the ingredients of this consumer product? * "Clean Cloth" is fictional; it does not represent any actual product. 5. The poison control center serving this region informs the doctor that Clean Cloth is 90% tetrachloroethylene and 10% inert propellant. Does the patient's use of this product pose any risk to her child? Explain. 6. How could a physician determine if a patient has been exposed to tetrachloroethylene? 7. What should a physician tell a patient about the hazards of tetrachloroethylene? 8. What other history will help determine whether the neurological symptoms of this patient are due to Clean Cloth? 9. The patient asks why her cousin, who uses Clean Cloth for the same purpose, has not been ill. What can her doctor tell her?

	10. The patient's laboratory tests show urinary trichloroacetic acid of 4.2 mg/L immediately after a 1-week exposure and slightly elevated aspartate aminotransferase (AST) and alanine aminotransferase (ALT). What do these results indicate? 11. If the patient wishes to continue using Clean Cloth, what could the doctor recommend? 12. What authorities should be notified if a product is used improperly in an industrial setting or by a large number of hobbyists?
Answers	1. The patient is 4 months postpartum. She has transient headaches, irritability, decreased ability to concentrate, slightly impaired coordination, possible alcohol use disorder, and possible post-partum depression. • The Case Presentation in the Pre-Course Knowledge Check covers this information 2. More information about the history of her headaches and her silk-screening hobby would help in diagnosing her symptoms. An accurate history of her current drinking pattern, using an assessment tool for alcohol or other drug-related problems, would also be helpful. Several screening and assessment instruments now are available in computer- or web-based versions [NIAAA 2005]. A toolkit designed to screen and diagnose patients with possible post-partum depression is available [ACOG 2009]. • Chapter 3, Section 3.1 covers this information 3. Because the patient is postpartum and possibly drinks alcohol in excess, the doctor should order tests to rule out anemia and thyroid problems, as well as tests checking renal and hepatic function. The following tests would also be appropriate: complete blood count, urinalysis, blood urea nitrogen (BUN) and serum creatinine; thyroid stimulating hormone (TSH) screening; and liver function. • Chapter 3, Section 3.1 covers this information 4. The doctor can first search this product online. Information in the Household Products Database is from a variety of publicly available sources including brand-specific labels and Safety Data Sheets (SDS) when available from manufacturers and manufacturers' web sites https://householdproducts.nlm.nih.gov/index.htm; the National Library of Medicine (NLM) TOXNET portal provides reliable information on toxicology, hazardous chemicals, environmental health, and toxic releases https://toxnet.nlm.nih.gov/; and the World Health Organization and the International Program on Chemical Safety maintain an international list of poison control centers http://www.who.int/ipcs/poisons/centre/en/. If searching these sites is unsuccessful, the doctor may call the regional poison control center to get help. In the United States, calling 1-800-222-1222 or

checking http://www.aapcc.org/ will provide an updated list of U.S. Poison Control Centers.

- Chapter 3, Section 3.4 covers this information.

5. Yes. Maternal exposure to tetrachloroethylene could transmit the chemical to the nursing infant because the solvent selectively concentrates in breast milk due to its lipophilicity. In addition, the infant could be exposed through inhalation if she is nearby when the patient is cleaning the fabric.

   - Chapter 1, Section 1.4 covers this information.

6. A reasonable first step would be to halt the exposure and determine if the symptoms resolve. Measuring tetrachloroethylene levels in breath, blood or urine would provide direct biologic indicators of tetrachloroethylene exposure. However, these laboratory studies are not rapidly available and do not change management priorities. Thus the diagnosis of hydrocarbon exposure is based upon clinical features [Lewander WJ and Aleguas, A. 2017].

   - Chapter 3, Section 3.1 covers this information.

7. The patient should understand the adverse effects of acute and chronic exposure to tetrachloroethylene and the potential long-term risks, particularly to nursing infants. She and her cousin should work in a well-ventilated area and use personal protective equipment, such as gloves, goggles, and a respirator that provide protection from tetrachloroethylene, when cleaning cloth during silk-screening [NIOSH 2018, OSHA 2005].

   - Chapter 2, Section 2.2, and Chapter 3, Section 3.4 cover this information.

8. Questions about symptoms and their association with using Clean Cloth might reveal a direct connection, as well as questions about the type and amount of ventilation and use of personal protective equipment.

   - Chapter 3, Section 3.1 covers this information.

   For example, the patient might respond that she sprays the cloth in late afternoon in a small garage and keeps the door closed to prevent dust from entering. She also recalls that one day last week, when it was hot, she felt particularly ill after spraying the cloth.

   - Chapter 3, Section 3.1 covers this information.

9. To answer this question, a review of the factors that could reduce the cousin's actual exposure might be helpful. These include intensity,

frequency, and duration of exposure; existing health conditions; etc. For example, the cousin

- might work outdoors or in a better ventilated area,
- might put rags soaked with the compound in a closed container, or
- might follow directions on safe product use.

Individual variability can also explain why some people become ill and others do not after similar exposures (e.g., breathing rate; effects of other exposures such as smoking, drugs, and alcohol on metabolic function; genetic differences in metabolic function).

- Chapter 1, Section 1.3 and Section 1.4 cover this information.

10. The urinary trichloroacetic acid level indicates a possible ambient air exposure of about 30 ppm tetrachloroethylene. It is a non-specific indicator though because exposure to other chemicals, such as 1,1,1-trichloroethane and trichloroethylene, also produce trichloroacetic acid in blood and urine. Although the lab results indicate possible exposure of tetrachloroethylene from using "Clean Cloth," the level might not be high enough to cause her symptoms. However, the patient could have also experienced periodic exposure to short-term levels much higher than this average level that could have caused her symptoms.

    The slightly elevated levels of AST and ALT are inconclusive for tetrachloroethylene exposure because of the confounding factor of alcohol consumption. An AST:ALT ratio greater than 1 (i.e., AST greater than ALT) tends to support an alcoholic-induced etiology. A ratio less than 1 (i.e., AST less than ALT) supports toxic, infectious, or other etiologies [AACC 2015]. Advising the patient to reduce alcohol consumption and counseling her about alcohol use disorder would be appropriate, as well as repeating liver function tests in several months.

    - Chapter 3, Section 3.1 covers this information.

11. The doctor could recommend using a less toxic cleaner. If the patient insists on using Clean Cloth, she could

    - reduce exposure to the product by using gloves, protective clothing, using a respirator or other PPE, be sure they are right for you and the chemical you work with,
    - ensure appropriate ventilation, and
    - get proper industrial hygiene consultation or other professional assistance.

    Since tetrachloroethylene crosses the placenta and can be found in breast milk; therefore, the fetus and nursing newborn could be at increased risk for

	adverse effects from maternal exposure. The tetrachloroethylene presently in her milk can be eliminated in several days if she continues to pump her breasts. • Chapter 3, Section 3.4 and Chapter 2, Section 2.1 cover this information. 12. The Occupational Safety and Health Administration (OSHA) has regulatory responsibility for the workplace and should be notified if employees might be dangerously exposed. Upon request, NIOSH could initiate a health hazard evaluation of the workplace. A product with hazardous potential used by a number of hobbyists should be reported to the local or state health department. • Chapter 3, Section 3.3 covers this information.

Chapter 1. Exposure Basics

Contents	Chapter 1 will cover the following topics: 1. What is tetrachloroethylene? 2. Where is tetrachloroethylene found? 3. What are the major routes of exposure to tetrachloroethylene?

Section 1.1. What Is Tetrachloroethylene?

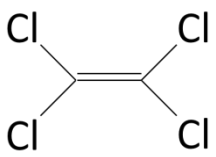
Learning objectives	After completing this section, you will be able to • define tetrachloroethylene and • describe uses of tetrachloroethylene.
Properties	• Tetrachloroethylene is a synthetic chemical. • It is a clear, colorless, nonflammable liquid with a sweet odor and a low aqueous solubility. • It is volatile and readily evaporates at room temperature. 

	Figure 1. Chemical structure of tetrachloroethylene - https://toxnet.nlm.nih.gov/cgi-bin/sis/search/a?dbs+hsdb:@term+@DOCNO+124
Use	A recent evaluation of end-use pattern for tetrachloroethylene [ATSDR 2015] estimated the following frequencies of use: • Chemical intermediates — 60% • Dry cleaning and textile processing — 18% • Metal degreasing — 18% • Oil refining catalyst regeneration — 2% • Miscellaneous uses including consumer products— 2% Other uses for tetrachloroethylene [EPA 2005] include • an intermediate in the synthesis of fluorocarbons, • an insulating/cooling fluid in electric transformers, • a component in typewriter correction fluids, • a veterinary medication against worms, and • a grain protectant and fumigant.
Synonyms	Chemical synonyms for tetrachloroethylene include • tetrachloroethene, • perchloroethylene, • 1,1,2,2-tetrachloroethylene, and • ethylene tetrachloride. Other commonly used names are • PCE, • perc, • perchlor, and • perclene.
Key point	Tetrachloroethylene is a synthetic chemical that is widely used for dry cleaning of fabrics and for metal degreasing, as well as in some consumer products.

Section 1.1 **Question #1**	Tetrachloroethylene is A. A clear liquid having low vapor pressure at room temperature. B. A volatile substance that readily evaporates at room temperature. C. An ingredient used mainly in consumer products in the United States. D. All of the above. *To review relevant content, see "Use" in Section 1.1.*

Section 1.2. Where Is Tetrachloroethylene Found?

Learning objective	After completing this section, you will be able to identify sources of tetrachloroethylene exposure.
Overview	People can be exposed to tetrachloroethylene from environmental and occupational sources and from consumer products. Tetrachloroethylene can be released into air, water, and soil at places where it is produced or used.
Environ-mental sources	**Air** Numerous studies have detected tetrachloroethylene in the air in rural, urban, and industrial areas in the United States. Although background levels are generally a fraction of a part per billion (ppb) in rural and remote areas, values in the parts per million (ppm) range are found in dry cleaning facilities [ATSDR 2015; NTP 2014]. Ambient air concentrations of tetrachloroethylene vary from source to source and with distance from the source. Near points of use, such as dry cleaners or industrial facilities, indoor exposure to tetrachloroethylene is more significant than outdoor exposure [EPA 2012a]. For instances, indoor air concentrations in apartments above a dry cleaning shop have been measured at up to 4.9 mg/m3 [Verberk and Scheffers 1980]. People living in New York City apartment buildings that also housed dry cleaners were exposed to higher levels of tetrachloroethylene (indoor air level of 27.5 $\mu g/m^3$) than were residents of buildings without a dry cleaner (2.3 $\mu g/m^3$) [Storm et al. 2013]. **Water** Tetrachloroethylene has been detected in • drinking water, • ground water, and • surface water. Some industries and building supplies can release tetrachloroethylene. In areas near sources of contamination, ground water and surface water concentrations can be considerably higher than in general areas [EPA 2012a]. **Soil** Contamination of soil can occur when tetrachloroethylene seeps from waste at disposal sites [ATSDR 2015]. **Food** Tetrachloroethylene has been detected in a variety of food items, including dairy products, meats, oils and fats, beverages, fruits, vegetables, fresh bread, fish, shellfish, and marine mammals [EPA 2012a; Gold LS et al. 2008; NTP 2014], but usually at low levels [ATSDR 2015]. Among about 280 food items periodically

	sampled as part of the U.S. Food and Drug Administration's Total Diet Study, tetrachloroethylene has been detected in 67 items (such as milk, cheese, meats, etc.) [FDA 2006].
Occupational sources	Tetrachloroethylene is a widely used solvent produced commercially for use in • dry cleaning, • textile processing, and • metal cleaning [Guyton et al. 2014]. Occupational exposure has been decreasing over the past several decades. For example, typical tetrachloroethylene concentrations in workplace air at dry-cleaning facilities were 350–700 mg/m^3 (about 50–100 ppm) in the 1970s and 70–350 mg/m^3 (about 10–50 ppm) in the 1980s. In 2003, the mean concentration of tetrachloroethylene at U.S. dry-cleaning facilities was 3.8 ppm [NTP 2014].
Consumer product sources	Tetrachloroethylene is found as an ingredient in a number of consumer products such as • adhesives, • stain removers, and • auto care products [U.S. National Library of Medicine 2015].
Environmental fate	Tetrachloroethylene is likely to enter the environment by fugitive air emissions from dry cleaning and metal degreasing industries and by spills or accidental releases to air, soil, or water [Howard 1990]. Tetrachloroethylene has relatively low solubility in water and has medium-to-high mobility in soil; thus, its residence time in surface environments is not expected to be more than a few days. However, it persists in the atmosphere for several months and can last for decades in the groundwater. Tetrachloroethylene can migrate through groundwater (or soil) up into the air of homes and buildings through vapor intrusion [ATSDR 2015].
Key points	• People can be exposed to tetrachloroethylene from environmental sources, occupational sources, and consumer products. • Tetrachloroethylene can last for decades in the groundwater and can migrate through groundwater (or soil) up into the air of homes and buildings through vapor intrusion.
Section 1.2 **Question #1**	People can be exposed to tetrachloroethylene in which of the following ways? A. Working in a building containing dry-cleaning facilities. B. Living in areas near metal cleaning operations. C. Using certain consumer products, such as adhesives or stain removers. D. All of the above. *To review relevant content, see Section 1.2.*

Section 1.3. What Are the Primary Routes of Exposure to Tetrachloroethylene?

Learning objective	After completing this section, you will be able to describe how people are exposed to tetrachloroethylene.
Overview	The primary routes of exposure to tetrachloroethylene for the general population are inhalation, including vapor intrusion from contaminated soil and water, and swallowing contaminated water [ATSDR 2015; EPA 2013c; Guyton et al. 2014]. Occupational exposure to tetrachloroethylene primarily occurs through inhalation and skin contact with this compound at workplaces that produce or use tetrachloroethylene [ATSDR 2015; Gold LS et al. 2008].
Inhalation	Inhalation is a major route of exposure to tetrachloroethylene. Inhaling tetrachloroethylene can be intentional or accidental. Exposure can occur through breathing contaminated air • during work with tetrachloroethylene or • while near others who are working with tetrachloroethylene. Tetrachloroethylene might also be inhaled from • accidental spills or product use in small, enclosed spaces; • clothing or newly dry-cleaned fabrics in homes; • landfills in which it was disposed; • releases to air and water by evaporation or emissions from industrial and dry-cleaning plants; • vapors formed from contaminated water used for bathing and laundering; • vapors rising from contaminated groundwater seeping into a basement or crawl space; and • evaporation from a spill on a person's skin or clothing.
Ingestion	Ingestion may occur through swallowing • food or • drinking water or • breast milk contaminated with tetrachloroethylene.
Skin	Absorption through skin can also be a route of tetrachloroethylene exposure in the workplace and among the general public. However, absorption is not an important route of exposure for most people because only 1% is absorbed through contact with intact skin [Nakai et al. 1999; NTP 2014; Wester et al. 2002].

Key point	The primary routes of exposure to tetrachloroethylene for the general population are inhalation, including vapor intrusion from contaminated soil and water, and swallowing contaminated water.
Section 1.3: Question #1	The primary routes of exposure to tetrachloroethylene for the general population are A. Inhalation + ingestion. B. Inhalation + dermal absorption. C. Ingestion + dermal absorption. D. Inhalation only. *To review relevant content, see Section 1.3.*

Section 1.4. Who Is at Risk for Exposure to Tetrachloroethylene?

Learning objective	After completing this section, you will be able to identify the populations with potentially high exposures to tetrachloroethylene.
Overview	Various segments of the population can be exposed to levels of tetrachloroethylene that are significantly above normal background concentrations [ATSDR 2015]. Persons who might be at greater risk of higher level exposure to PCE include • workers in industries such as dry cleaning, machining, and electronics, as well as people who use tetrachloroethylene-containing products, • people living with dry cleaning workers, • people residing near contaminated sites or dry cleaning locations, and • the fetus and nursing newborn of women exposed to tetrachloroethylene through transfer to the placenta or breast milk, respectively.
Workers	Occupational exposures are by far the source of the highest-level exposures to tetrachloroethylene. Exposure to tetrachloroethylene occurs most often in the dry cleaning industry, but substantial exposures also occur in metal manufacturing industries through degreasing processes, and from a variety of uses in several other industries (such as manufacturing apparel, other textile products, electronic components and accessories; paper and pulp plants; and printing and publishing industries, etc.) [Gold LS et al. 2008].
Workers' family members	Indoor air of exposed dry-cleaning workers' homes can contain levels of tetrachloroethylene much higher than those in the homes of non-exposed workers [Aggazzotti et al. 1994a; Aggazzotti et al. 1994b]. A survey of 30 such homes found indoor tetrachloroethylene levels of 34–3,000 micrograms per cubic meter ($\mu g/m^3$) (5.0–442 ppb), which was significantly higher than levels in control homes (1–16 $\mu g/m^3$ or 0.1–2.4 ppb). These higher exposures were attributed to clothing worn home from work and workers' breath, since 70% or more of an oral or inhaled dose of tetrachloroethylene is eliminated in expired air.

Consumers	Exposure to tetrachloroethylene can occur from contact with certain consumer products. Tetrachloroethylene is found as an ingredient in some consumer products such as adhesives, stain removers, and auto care products [HHS 2015]. People who use tetrachloroethylene-containing products in a poorly ventilated area without proper use of personal protective equipment have an increased likelihood of exposure. Clothes, drapes, and other dry-cleaned fabrics can also serve as a source of tetrachloroethylene release, resulting in elevated indoor air levels. One study found that newly dry-cleaned garments stored in a residential closet resulted in tetrachloroethylene levels of 0.5–2.9 milligrams per cubic meter (mg/m^3) (74–428 ppb) in the closet after one day. Initial "airing out" of the clothes for 4 to 8 hours had little effect on the resulting emissions [Tichenor et al. 1990]. A 2-year-old boy was found dead 1.5 hours after he was placed in his room with curtains that had been incorrectly dry-cleaned in a coin-operated dry cleaning machine [Garnier et al. 1996].
Special populations	People who live near contaminated sites or dry cleaning locations might be exposed to higher levels than the general population. Contaminated water used for bathing and laundering can emit vapors that increase indoor air levels of tetrachloroethylene. People living in New York City apartment buildings that also housed dry cleaners were exposed to higher levels of tetrachloroethylene (indoor air level of 27.5 $\mu g/m^3$) than were residents of buildings without a dry cleaner (2.3 $\mu g/m^3$) [Storm et al. 2013].
Fetus and nursing newborn of women at risk for exposure	Data from animal and human studies indicate that tetrachloroethylene crosses the placenta, placing the fetus at risk of exposure [Fredriksson et al. 1993; Ghantous et al. 1986; Van der Gulden and Zielhuis 1989]. Tetrachloroethylene, like many chlorinated hydrocarbons, can be transmitted in breast milk [EPA 2012a]. In one case report, a nursing mother was repeatedly exposed to tetrachloroethylene vapors during lunch-hour visits with her husband at a dry-cleaning plant. She had tetrachloroethylene levels of 300 micrograms per deciliter (μg/dL) in blood and 1,000 μg/dL in breast milk. The nursing infant developed obstructive jaundice, possibly as a result of tetrachloroethylene exposure [Bagnell and Ellenberger 1977].
Key points	• Workers in industries such as dry cleaning, machining, and electronics, as well as people who use tetrachloroethylene-containing products, have an increased likelihood of exposure. • Family members of exposed workers are subject to higher risk for exposure to tetrachloroethylene. • People who live near contaminated sites or dry cleaning locations might be exposed to higher levels than the general population. • Tetrachloroethylene crosses the placenta and can be found in breast milk; therefore, the fetus and nursing newborn could be at increased risk for exposure via maternal exposure.

Section 1.4: Question #1	Who of the following is at risk for tetrachloroethylene exposure? A. Newborns of nursing mothers who work at a dry-cleaning plant. B. Consumers who use spot remover. C. Machine operators in a dry-cleaning plant. D. All of the above. *To review relevant content, see Section 1.4.*

Chapter 2. Biological and Clinical Effects of Tetrachloroethylene Exposure

Contents	Chapter 2 will cover the following topics: Section 2.1. Biological fate of tetrachloroethylene Section 2.2. Clinical effects

Section 2.1. Biological fate of tetrachloroethylene

Learning objective	After completing this section, you will be able to explain the major pathways of tetrachloroethylene metabolism in the body.
Overview	Tetrachloroethylene is rapidly and extensively absorbed after inhalation and oral exposure. Once absorbed, tetrachloroethylene is rapidly distributed throughout the body. The limited metabolism of tetrachloroethylene occurs through two pathways, oxidation via cytochrome P-450 and conjugation with glutathione. These pathways produce many metabolites, including some known to be cytotoxic, mutagenic, or both. The elimination of an absorbed dose of tetrachloroethylene occurs primarily in expired air as the parent compound.
Absorption and distribution	The lungs absorb about 64%–100% of an inhaled dose of tetrachloroethylene [Chiu et al. 2007; Monster et al. 1979], and the gut absorbs almost 100% of an oral dose of tetrachloroethylene [Dallas et al. 1994a; Dallas et al. 1995)]. Only 1% is absorbed through contact with intact skin [Nakai et al. 1999; Wester et al. 2002]. After tetrachloroethylene is absorbed, it is readily distributed to all body tissues. Because it is highly lipid soluble, tetrachloroethylene tends to concentrate primarily in adipose tissue [Dallas et al. 1994a; Dallas et al. 1994b]. Tetrachloroethylene is also concentrated in breast milk [Schreiber 1997; Schreiber et al. 2002].

Metabolism and toxicity	Tetrachloroethylene can be sequestered in fat because of its high lipid solubility; therefore, not all metabolism is evident in short sampling periods [EPA 2012a]. About 1%–3% of the estimated amount inhaled was metabolized to trichloroacetic acid (TCA) and other chlorinated oxidation products in a short period. Additional tetrachloroethylene (as much as 20% or more of the dose) may be metabolized over a longer period [Chiu et al. 2007; EPA 2012a; Monster et al. 1979]. These estimates appear to be consistent with the eliminated percentage of an oral or inhaled dose of tetrachloroethylene (see below). Metabolism of tetrachloroethylene yields multiple toxic metabolites through two main pathways [Guyton et al. 2014; Lash and Parker 2001]: 1. **Oxidation via cytochrome P450—**Metabolism via cytochrome P450 enzymes occurs predominantly in the liver. The pathway generates trichloroacetic acid (TCA) and dichloroacetic acid (DCA) as metabolites of tetrachloroethylene. 2. **Conjugation with glutathione—**Tetrachloroethylene conjugation with glutathione (GSH) in the liver or kidney forms trichlorovinyl glutathione (TCVG), which is further processed in the kidney, forming the S-trichlorovinyl-L-cysteine (TCVC). Studies have shown that these metabolites are cytotoxic, mutagenic, or both [Guyton et al. 2014; Lash and Parker 2001; NRC (National Research Council) 2010]. The parent compound tetrachloroethylene is also a likely contributing factor to neurotoxicity, particularly central nervous system (CNS) effects [Boyes et al. 2009; EPA 2012a].
Elimination	Mass-balance studies in rats with ^{14}C-labeled tetrachloroethylene indicated that 70% or more of an oral or inhaled dose can be recovered in expired air as the parent compound. The next important excreted fraction in the form of trichloroacetic acid occurs in urine and feces, collectively accounting for up to 23% of an administered dose. A small portion of the dose (less than 3%) may be converted to CO_2 and exhaled [Frantz 1983; NRC (National Research Council) 2010; Pegg et al. 1979]. The half-life of tetrachloroethylene in three major body compartments is calculated [Monster et al. 1979] to be • 12–16 hours for vessel-rich tissues such as brain, heart, lungs, kidneys, and liver; • 30–40 hours for poorly perfused tissues such as muscle; and • 55–65 hours for adipose tissue.
Key points	• Tetrachloroethylene rapidly absorbs into the bloodstream after oral and inhalation exposures.

	• 70% or more of an oral or inhaled dose can be recovered in expired air as the parent compound. • In general, metabolism of tetrachloroethylene yields multiple metabolites through two distinct pathways. These metabolites are associated with liver toxicity, renal toxicity, and carcinogenicity.
Section 2.1: Question #1	After being absorbed, most of the inhaled tetrachloroethylene is A. Metabolized in the liver. B. Eliminated unchanged by the lungs. C. Metabolized in the kidney. D. Excreted in urine as trichloroacetic acid (TCA) and other chlorinated oxidation products. *To review relevant content, see Section 2.1.*

Section 2.2. Clinical effects

Learning objective	After completing this section, you will be able to describe the clinical effects associated with tetrachloroethylene exposure.
Overview	The central nervous system, liver, kidney, and reproductive system are target organs of tetrachloroethylene toxicity [EPA 2012b]. Tetrachloroethylene hepatic effects are thought to result from oxidative metabolites [Buben and O'Flaherty 1985], whereas metabolites resulting from glutathione conjugation are thought to cause kidney effects [Lash and Parker 2001]. Tetrachloroethylene itself has been presumed to cause neurological effects [Guyton et al. 2014]. Epidemiologic studies have shown associations between tetrachloroethylene exposure and several types of cancer.
Neurological effects	Neurotoxicity is a sensitive outcome seen in humans and experimental animals exposed to tetrachloroethylene by inhalation or ingestion. A wide range of effects on neurologic function have been observed in humans after acute and chronic exposure to tetrachloroethylene. Vision and cognitive function are most commonly affected [EPA 2012a; Guyton et al. 2014; Schreiber et al. 2002]. Symptoms temporally related to exposure are a function of the anesthetic property of organic solvents. Specifically, dizziness, light-headedness, impaired concentration, and headaches that have a temporal relationship to solvent exposure are likely the result of the acute CNS effects [Meredith et al. 1989; Rom 2007]. These symptoms are likely to resolve quickly after moving from the contaminated environment to fresh air and might significantly improve or resolve by the time a healthcare professional evaluates the patient.
Hepatic effects	Hepatotoxic effects such as hepatomegaly, hepatocellular damage, and elevations of gamma-glutamyltransferase and bilirubin degradation byproducts have been observed after acute high-level exposure to tetrachloroethylene [ATSDR 2015; EPA 2012a; Lash and Parker 2001]. Some cross-sectional studies of occupationally exposed dry cleaning workers [Brodkin et al. 1995; Gennari et al. 1992] showed indications of liver toxicity. Mild to moderate hepatic parenchymal changes occur more frequently in workers exposed to tetrachloroethylene than in populations not exposed to chemical solvents. Studies have also reported liver toxicity in multiple animal species as a result of inhalation and oral exposures to tetrachloroethylene [ATSDR 2015; EPA 2012a; Lash and Parker 2001].

Renal effects	Several studies have described nephrotoxic effects in humans [ATSDR 2015, 2017; EPA 2012a; Lash and Parker 2001; Mutti et al. 1992; Verplanke et al. 1999]. Hematuria and proteinuria have been associated with anesthetic concentrations of tetrachloroethylene. Chronically exposed dry-cleaning workers have increased urinary levels of lysozymes, β2-microglobulin, and other low-molecular-weight proteins, suggesting tubular damage. Adverse effects on the kidneys have been observed in studies of animals exposed to high concentrations of tetrachloroethylene by inhalation, oral gavage, and intraperitoneal injection of tetrachloroethylene metabolites [ATSDR 2015; EPA 2012a; Lash and Parker 2001].
Reproductive effects	A number of studies of tetrachloroethylene exposure have evaluated reproductive outcomes, including • menstrual disorders, • altered semen quality, • reduced fertility, • increased time to pregnancy, and • adverse pregnancy outcomes (such as spontaneous abortion, low birth weight or gestational age, and stillbirth). However, the evidence is inconclusive [ATSDR 2015; EPA 2012a]. Studies of tetrachloroethylene in drinking water have reported that exposure during pregnancy is associated with low birth weight and oral clefts [Aschengrau et al. 2009; Bove et al. 1995; Sonnenfeld et al. 2001]. However, due to several limitations of these studies, firm conclusions cannot be drawn [EPA 2012a]. Tetrachloroethylene crosses the placenta and can be found in breast milk; therefore, the fetus and nursing newborn might be at increased risk for adverse effects from maternal exposure [Bagnell and Ellenberger 1977; Schreiber 1993; Sheldon L and Zelon H 1985]. Evidence from a limited number of well-conducted reproductive studies in laboratory animals suggests that tetrachloroethylene is a potential female reproductive toxicant, resulting in decreased number of liveborn pups, increased pre-and post-implantation loss, and increased resorptions [ATSDR 2015].

Carcinogenic effects	The available epidemiologic studies provide a pattern of evidence associating tetrachloroethylene exposure and several types of cancer, specifically bladder cancer [Aschengrau et al. 1993; Blair et al. 2003; Lynge et al. 2006; Pesch et al. 2000], non-Hodgkin's lymphoma [Anttila et al. 1995; Radican et al. 2008; Seldén 2011], and multiple myeloma [Gold L et al. 2010; Radican et al. 2008]. In a recent report, ATSDR concludes that information is insufficient to determine whether a causal association exists for tetrachloroethylene and multiple myeloma [ATSDR 2017]. Other epidemiologic studies suggest possible associations with other cancer sites (bone marrow, esophageal, kidney, lung, liver, cervical, and breast cancer), but the data are more limited or inconsistent [ATSDR 2015, 2017; EPA 2012a]. The administration of PCE, either by ingestion or by inhalation to sexually mature rats and mice, increases tumor incidence (such as mononuclear cell leukemia, kidney, or hepatocellular tumors) [Japan Industrial Safety Association (JISA) 1993; National Cancer Institute 1977; National Toxicology Program (NTP) 1986]. The International Agency for Research on Cancer (IARC) classified tetrachloroethylene as a Group 2A agent— "probably carcinogenic to humans" [IARC 1995], The U.S. Department of Health and Human Services believes it is "reasonably anticipated to be a human carcinogen" [NTP 2014]. The U.S. Environmental Protection Agency (EPA) characterizes tetrachloroethylene as "likely to be carcinogenic to humans" [EPA 2012a]. These evaluations are based on the findings of limited evidence in humans and sufficient evidence of carcinogenicity in experimental animals.
Other clinical effects	The available studies of immunological effects in humans exposed to tetrachloroethylene provide suggestive evidence for alterations in blood biomarkers (e.g., IgE and cytokine levels) related to inflammation and hypersensitivity. However, the data are limited and exposure concentrations are uncertain. Evidence suggests subtle perturbations of the immune system in animals exposed to tetrachloroethylene, but the data are limited and the relevance to humans is uncertain at present; further research is needed [ATSDR 2015]. Chemical burns characterized by severe cutaneous erythema, blistering, and sloughing have resulted from prolonged (more than 5 hours) accidental contact exposure to tetrachloroethylene used in dry-cleaning operations [ATSDR 2015].
Key points	• Neurotoxicity is a sensitive outcome of either oral or inhalational exposure to tetrachloroethylene in humans and experimental animals. • Tetrachloroethylene may also adversely affect the liver and kidneys. • Studies suggest tetrachloroethylene exposure may cause adverse reproductive outcomes. It might harm the fetus and newborn through maternal exposure.

	• IARC has classified tetrachloroethylene as "probably carcinogenic to humans" (Group 2A).
Section 2.2: **Question #1**	Which one of the following statements is **NOT** true? A. Hepatic and renal toxicity can occur in humans exposed to tetrachloroethylene. B. CNS effects might be reversible on cessation of exposure. C. The fetus and nursing newborn could be at increased risk for adverse effects from maternal exposure to tetrachloroethylene. D. Tetrachloroethylene is probably not a carcinogen to humans. *To review relevant content, see Section 2.1.*

Chapter 3. Diagnosis, Treatment, and Prevention

Contents	Chapter 3 covers the following topics: Section 3.1. Evaluation and diagnosis Section 3.2. Treatment Section 3.3. Regulations and guidelines Section 3.4. Counseling and prevention

Section 3.1. Evaluation and diagnosis

Learning objectives	After completing this section, you will be able to • describe what is included in the initial history of patients potentially exposed to tetrachloroethylene, • describe what is included in the physical examination of patients potentially exposed to tetrachloroethylene, • describe possible clinical symptoms in patients exposed to tetrachloroethylene, and • identify tests that can help diagnose tetrachloroethylene toxicity.
Overview	Symptoms and signs potentially associated with tetrachloroethylene exposure are nonspecific, making a careful medical and exposure history essential to diagnosis. The initial history and physical examination of patients potentially exposed to tetrachloroethylene can be used to • determine possible sources and pathways of exposure to tetrachloroethylene, • detect symptoms and signs attributable to tetrachloroethylene exposure, and

	• reveal history of any preexisting or underlying condition(s) that might complicate the diagnostic and clinical approach to the patient.
Patient history	An exposure history* should be part of the patient history. Taking an exposure history may enable physicians to • make more accurate diagnoses, • influence the course of disease by stopping current exposure, • prevent disease in others by avoiding future exposure, and • prompt workplace evaluations and worker protection. An exposure history should cover occupational and non-occupational tetrachloroethylene exposure risks. If you suspect a temporal association between symptoms and exposure to certain products, try to identify the specific chemical ingredients involved. **Environmental exposure history** An environmental exposure history (non-occupational) for tetrachloroethylene includes • type of water supply, • location and duration of residence, • proximity to industry and National Priorities List sites, and • patient's hobbies. Gather any additional information regarding history of exposure to other potentially toxic agents, including medications and alcohol. **Occupational exposure history** The patient's occupational history is crucial. For each job held, the exposure history should include • Company name and location • Job title (previous work and type of occupation) • Description of chemical processes used • Known toxic agents • History of worker illness • Enclosure of solvent-related processes • Use of a hood or other ventilation • Use of personal protective equipment (such as respirator and gloves) Collect information on the specific constituents of the solvent-containing materials and other potentially hazardous substances used. You might need to ask employers, suppliers, or manufacturers for the safety data sheet (SDS) (formerly known as material safety data sheet [MSDS]). Determine the patient's use of personal

	protective equipment. The occupational history should also include the patient's general assessment of the hygienic conditions of the work setting, including the availability of separate washing, changing, and eating facilities. Also ask the patient about potential exposure(s) from the activities of coworkers. **Medical history** Medical history and review of body systems should include assessment of current and past diagnoses or symptoms of diseases of the • neurologic, • hepatic, • renal, and • reproductive systems. Also consider the association between solvent exposure and health conditions [Rom 2007], such as • glomerulonephritis, • contact dermatitis, • cognitive impairment, and • peripheral neuropathy. Identify the patient's complaints in terms of • onset, • duration, • frequency, and • intensity. Note the time of patient's last exposure to a suspected chemical. A temporal relationship between onset of symptoms and work or other activity could provide important diagnostic clues. *ATSDR has developed other CSEMs, including "Taking an Exposure History" and "Taking a Pediatric Exposure History." To view these CSEMs, please go to http://www.atsdr.cdc.gov/csem/.
Physical examination	When performing the physical examination, focus on the major organ systems that tetrachloroethylene exposure is likely to affect (e.g., CNS, hepatic, renal, reproductive, and skin) [Rom 2007]. You might see subclinical, delayed, or individual variability in the initial presentation. Record vital signs, noting any abnormalities of heart rate or rhythm. Examine the head, eyes, ears, nose, and throat, noting any inflammation or irritation. Inspect the skin, especially the hands, for signs of

	• redness, • drying, • cracking, or • fissuring. Also note signs of hepatic dysfunction (e.g., jaundice). Chest examination should include assessment of the heart and lungs. Abdominal exam should include palpation for liver and spleen size (i.e., hepatomegaly, hepatosplenomegaly, etc.) and tenderness. Conduct a mental status examination to evaluate • alertness, • orientation, • cognition, and • short-term memory. Assess peripheral nerve function by evaluating • proprioception, • deep tendon reflexes, • motor strength, • postural stability (Romberg test), and • sensitivity to vibration, light touch, and pin prick.
Signs and symptoms: **Acute exposure**	The onset, intensity, and duration of symptoms can vary among identically exposed persons. Many factors influence the variability of toxicity, including respiratory rate, target organ sensitivity, body fat content, and general health. CNS symptoms can be similar to those of ethanol inebriation. Patients with some of the following symptoms, grouped by system, might have acute high-level tetrachloroethylene exposure: Nervous system • Confusion • Dizziness • Euphoria • Forgetfulness • Headache • Irritability • Light-headedness • Loss of consciousness • Loss of coordination

	• Sleepiness • Slurred speech Gastrointestinal • Nausea Ear, nose, and throat • Cough • Eye and nose irritation • Upper airway irritation
Signs and symptoms: **Chronic exposure**	Mild CNS symptoms have reportedly resulted from exposure to tetrachloroethylene-containing household products in confined spaces and after exposure in industrial settings. Reported symptoms from chronic inhalation exposure have included • ataxia, • disorientation, • irritability, • persistent headache, • short-term memory deficits, and • sleep disturbances. 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. You may also note signs of hepatic dysfunction (e.g., jaundice). Tetrachloroethylene's defatting action on skin may cause dermatitis, thereby predisposing the skin to infection.
Laboratory tests: Introduction	Tetrachloroethylene may be measured to confirm tetrachloroethylene exposure. Significant exposure to tetrachloroethylene can result in elevated values of routine laboratory tests, including renal and liver function tests, although they are not specific to tetrachloroethylene exposure.
Direct biologic indicators	For acute exposures, tetrachloroethylene in expired air can be measured although it might also be detected in blood or urine [Baselt 1997; Imbriani et al, 1988]. Although tetrachloroethylene can be measured in breath, blood or urine, these laboratory studies are not rapidly available and do not change management priorities. Thus the diagnosis of hydrocarbon exposure is based upon clinical features [Lewander WJ and Aleguas, A. 2017]. For chronic exposures, urine or blood levels of trichloroacetic acid (TCA) can be measured. However, exposure to other chemicals, such as 1,1,1-trichloroethane and trichloroethylene, also produce trichloroacetic acid in blood and urine, as does use

	of the prescription sedative chloral hydrate. Thus, the presence of this particular metabolite is not specific to tetrachloroethylene exposure. In a random sampling of 2,735 participants in the 2007–2008 U.S. National Health and Nutrition Examination Survey (NHANES), blood concentrations of tetrachloroethylene ranged from below the limit of detection up to 0.094 ng/m [CDC 2017].
Indirect biologic indicators	Although tetrachloroethylene can cause upper airway irritation and coughing, chest radiograph and pulmonary function tests are usually normal. In general, results of routine laboratory tests, including renal and liver function tests, will also be normal, unless the patient has had an exposure significant enough to cause concurrent neurological symptoms. One study looked at subclinical hepatotoxicity in workers exposed to tetrachloroethylene in dry cleaning establishments. It compared the sensitivity of hepatic parenchymal ultrasonography with measurements of serum transaminases as liver biomarkers [Brodkin et al. 1995; Lash and Parker 2001]. The study found mild to moderate changes in hepatic parenchyma (i.e., diffuse parenchymal changes in echogenicity) more frequently in workers exposed to tetrachloroethylene than in a control population not exposed to tetrachloroethylene. In contrast, the incidence of increased serum alanine aminotransferase activity in these same workers was much less than that of the changes in ultrasonography. When assessing hepatic parenchymal changes determined by ultrasonography, the clinicians should also take into account of other hepatotoxic factors when making the final clinical assessment of hepatotoxicity from tetrachloroethylene. Such factors can include prescription medications, alcoholism, nutrition, genetics, and preexisting disease of the liver [Brautbar and Williams 2002; Brodkin et al. 1995].

Indirect biologic indicator: **Baseline**	Conduct the following testing immediately to establish baseline values if acute exposure to tetrachloroethylene has resulted in marked CNS symptoms such as syncope • Liver function • Blood urea nitrogen (BUN) • Serum creatinine • Urinalysis Repeat testing after several days to monitor for possible effects. Liver function tests should include • alkaline phosphatase, • ALT (SGPT), • AST (SGOT), • bilirubin, and • lactate dehydrogenase. Transient elevations of serum levels of liver enzymes have been reported in tetrachloroethylene exposure, but documented hepatic necrosis is rare. If enzyme levels remain elevated, consider other causes of hepatic dysfunction and initiate appropriate clinical evaluation. Always consider alcohol consumption when interpreting liver function test results. Neuropsychological testing might be useful for comparing exposed occupational populations to non-exposed control groups. Contacting an expert in environmental medicine may provide information, assistance, and referral for clinical evaluation if the exposure history verifies environmental exposures.
Key points	• An exposure history should be part of the patient history. • Establishing a temporal relationship between the patient's signs and symptoms and exposure to tetrachloroethylene can aid in diagnosis. • Patients exposed to tetrachloroethylene by any route predominantly exhibit CNS symptoms. • Although testing may measure tetrachloroethylene in breath, blood, urine, breast milk, and adipose tissue, etc., this testing is mainly useful in research and not in routine clinical evaluation.

Section 3.1: **Question #1**	The primary focus of the patient exposure history for tetrachloroethylene includes which of the following? A. Evaluate general health. B. Determine patient's organ system status. C. Explore important clues about causation. D. All of the above. *To review relevant content, see "Patient history" in this section (3.1).*
Section 3.1: **Question #2**	On patient examination, short-term memory loss, if associated with acute tetrachloroethylene exposure, is generally A. Irreversible. B. Reversible. C. Similar to other forms of dementia. D. The initial symptom of acute exposure. *To review relevant content, see "Physical examination" in this section (3.1)*
Section 3.1: **Question #3**	Which of the following indicator(s) confirm(s) tetrachloroethylene exposure? A. Trichloroacetic acid in blood or urine. B. Tetrachloroethylene in breath, blood, or urine. C. Elevated values of renal and liver function tests. D. Hepatic ultrasound. *To review relevant content, see "Direct biologic indicators" in this section (3.1).*

Section 3.2. Treatment

Learning objective	After completing this section, you will be able to describe treatment strategies for patients with tetrachloroethylene poisoning.
Overview	Tetrachloroethylene poisoning has no antidote. Treatment consists of removing the patient from the exposure and supporting respiratory and cardiovascular functions.
Acute exposure	Tetrachloroethylene poisoning has no antidote. Treatment is supportive. In all suspected cases, remove the patient from the source of exposure. Provide standard support for respiratory and cardiovascular functions when needed. Additional recommendations include • restricting use of alcohol or other CNS depressant medication, • removing contaminated clothing, • washing affected areas with mild soap and copious amounts of water, • moving from the contaminated area and/or • maintaining good ventilation.

Chronic exposure	Symptoms related to chronic exposure tend to worsen during exposure and improve when exposure stops, such as during vacation or after a job transfer. Consider other causes for symptoms if no clear association between symptoms and exposure exists. The level of exposure either must be reduced or the source eliminated for persons with tetrachloroethylene toxicity. Depending on the setting, this might be accomplished by • using an agent less hazardous than tetrachloroethylene or • increasing air ventilation.
Key points	• Tetrachloroethylene toxicity has no antidote; supportive measures should be administered. • In all suspected cases, removal from exposure should reduce or eliminate symptoms.
Section 3.2: Question #1	Which one of the following statements is **NOT** correct? A. Symptoms related to chronic exposure tend to worsen during exposure and improve when exposure ceases. B. The patient should avoid use of alcohol or other CNS depressant medication. C. Supportive care includes providing adequate ventilation and air circulation. D. Tetrachloroethylene poisoning has a specific antidote. *To review relevant content, see this entire section (3.2).*

Section 3.3. Regulations and guidelines

Learning objectives	After completing this section, you will be able to • identify existing standards and guidelines for tetrachloroethylene in the environment and • identify existing standards and guidelines for tetrachloroethylene in the workplace.
Overview	The federal government has developed regulations and guidelines for tetrachloroethylene to protect the public and workers from potential adverse health effects from exposure. Federal regulations that eliminate the use of tetrachloroethylene in dry cleaning in urban locations will go into effect in December 2020 [CMR 2008].

U.S. Federal regulations and guidelines

Air

EPA has designated tetrachloroethylene as a hazardous air pollutant under the Clean Air Act [EPA 2013b].

Water

The current EPA drinking water regulation for tetrachloroethylene is 5 ppb (= 5 µg/L) [EPA 2013a].

Food

The U.S. Food and Drug Administration (FDA) [FDA 2017] monitors bottled water and has established an acceptable level of 5 µg/L for bottled water.

Table 1. Standards and Regulations for Tetrachloroethylene.

Agency	Focus	Level*	Comments
American Conference of Governmental Industrial Hygienists (ACGIH)	Air: workplace	25 ppm	Advisory; TLV/TWA[†] STEL[‡] of 100 ppm
National Institute for Occupational Safety and Health (NIOSH)	Air: workplace	Not available	Advisory; lowest feasible level because of carcinogenicity
Occupational Safety and Health Administration (OSHA)	Air: workplace	100 ppm	Regulation; PEL[§] over an 8-hour workday
U.S. Environmental Protection Agency (EPA)	Air: environment	None	Listed as a hazardous air pollutant under Section 112 of the Clean Air Act
U.S. Environmental Protection Agency (EPA)	Water: environment	5 ppb	Regulation; maximum level allowed in drinking water
U.S. Food and Drug Administration (FDA)	Food: bottled drinking water	5 µg/L	Regulation

*ppm: parts per million; ppb: parts per billion.

[†]TLV/TWA (threshold limit value/time-weighted average): time-weighted average concentration of exposure for nearly all work during a normal 8-hour workday or 40-hour workweek.

	[‡]STEL (short-term exposure limit): usually a 15-minute sampling period. [§]PEL (permissible exposure limit): highest level of exposure, averaged over a normal workday.
Environmental and workplace air standards	**Environmental** EPA regulates three types of tetrachloroethylene dry cleaners under the Clean Air Act 1. Large industrial and commercial dry cleaners 2. Freestanding small dry cleaners 3. Small dry cleaners in apartment buildings EPA has required operators to reduce emissions from dry cleaners and has established a final rule on the phase out of tetrachloroethylene use in dry cleaners in residential areas by December 21, 2020. Currently, approximately 28,000 U.S. dry cleaners use tetrachloroethylene [ATSDR 2015]. **Occupational** OSHA has established a permissible exposure limit (PEL) in workplace air of 100 ppm measured as an 8-hour time-weighted average (TWA) [OSHA 2013] (Table 1). NIOSH recommends treating tetrachloroethylene in the workplace as a potential human carcinogen and reducing occupational exposure to the lowest feasible level [NIOSH 2013]. The American Conference of Governmental Industrial Hygienists [ACGIH 2016] recommends a threshold limit value (TLV) of 25 ppm for an 8-hour TWA and a short-term exposure limit (STEL) of 100 ppm.
Key points	• EPA has designated tetrachloroethylene as a hazardous air pollutant under the Clean Air Act. • The current EPA and FDA tap and bottled water regulation for tetrachloroethylene is 5 µg/L. Federal regulations have gradually reduced the use of tetrachloroethylene and will eliminate the use of tetrachloroethylene in dry cleaning in urban locations in December 2020. • NIOSH recommends treating tetrachloroethylene in the workplace as a potential human carcinogen and reducing occupational exposure to the lowest feasible level.

Section 3.3: **Question #1**	Which of the following statements regarding U.S. regulations and guidelines for tetrachloroethylene is **NOT** true? A. NIOSH recommends treating tetrachloroethylene in the workplace as a potential human carcinogen and reducing occupational exposure to the lowest feasible level. B. EPA does not require operators to begin reducing tetrachloroethylene emissions from dry cleaners until December 21, 2020. C. Under the Clean Air Act, EPA regulates three types of tetrachloroethylene dry cleaners. D. ACGIH recommends a threshold limit value for workplace air exposure. *To review relevant content, see this entire section (3.3).*

Section 3.4. Counseling and prevention

Learning objectives	After completing this section, you will be able to • identify suitable self-care for patients exposed to tetrachloroethylene, • identify clinical follow-up for patients exposed to tetrachloroethylene, and • describe how to counsel patients appropriately on how to avoid further exposure to tetrachloroethylene.
Overview	All patients exposed to tetrachloroethylene need basic guidance on • self-care, so they can minimize further risks and avoid complications to the extent possible and • clinical follow-up, so they understand when and why to return for further medical attention.
Self-care	Advise patients to avoid exposures and conditions that might further increase their risk for disease or worsen their existing condition(s). High levels of exposure can occur during cleanup of contaminated equipment and spills, and might require use of an approved full-face piece self-contained breathing apparatus or similar device. Industries and businesses should establish procedures for spill cleanup in advance, including capping all containers of liquid tetrachloroethylene and storing rags soaked with tetrachloroethylene in sealed containers. In occupational exposures, the law requires employers or manufacturers to provide pertinent safety data sheets (SDS). The SDS for a chemical product lists its ingredients, describes their potential toxicity, and suggests precautions for safe use. Advice on self-care for the patient might include the following: **At home**

	• Use safer alternatives to products with tetrachloroethylene • When using products containing tetrachloroethylene, ensure plenty of airflow/ventilation (e.g. opening all windows and using fans) • Use appropriate PPE that protects against tetrachloroethylene (e.g., wear a proper respirator or protective gloves, or both) when using products that contain tetrachloroethylene [NIOSH 2018, OSHA 2005] **At work** • OSHA's Hazard Communication Standard [OSHA 2012] requires employers to provide labeling, SDS, and safety training on use of chemicals in the workplace. • Be sure to use the employer-supplied personal protective equipment: gloves, goggles, mask, and respirator as recommended. • Read employer-provided SDS on products that you use. • Be sure all containers of chemicals used at work are properly labeled. • Attend employer-provided training on how to use chemicals safely at work.
Clinical follow up	Scientific studies have implicated tetrachloroethylene as a probable cause of several types of cancers, including bladder cancer and non-Hodgkin's lymphoma. Periodic clinical evaluation may help detect abnormalities at an early stage, if they occur. This would also be true for other tetrachloroethylene-related health effects. Consultation with a specialist in occupational and environmental medicine or others with expertise and experience treating patients exposed to tetrachloroethylene may help you develop a periodic monitoring plan, as appropriate. Patient counseling on the importance of exposure mitigation and ways to reduce exposure risk would be prudent, along with instructions to consult you or another physician if concerns about exposure arise. Advise patients to consult you or another physician if they develop signs or symptoms of • CNS disorders or • other health changes (especially those possibly related to liver and kidney problems).

Additional information and resources	Please refer to the following online resources for more information on the adverse effects of tetrachloroethylene, the treatment of tetrachloroethylene poisoning, and management of persons exposed to tetrachloroethylene. You may also contact ATSDR (see URLs provided below), your state and local health departments, and university medical centers. **For emergency situations, call CDC Emergency Response: 770-488-7100. To report an oil or chemical spill, call EPA Emergency Response: 800-424-8802.** For non-emergency situations, call CDC-INFO: 1-800-CDC-INFO (1-800-232-4636); TTY 888-232-6348 24 hours/day email: cdcinfo@cdc.gov. **PLEASE NOTE**: ATSDR cannot respond to questions about individual medical cases, provide second opinions, or make specific recommendations regarding therapy. Patients should address those issues directly with a health care provider. ATSDR Toxicological Profile for Tetrachloroethylene https://www.atsdr.cdc.gov/toxprofiles/TP.asp?id=265&tid=48 ToxFAQs™ for Tetrachloroethylene https://www.atsdr.cdc.gov/toxfaqs/TF.asp?id=264&tid=48 **Other Sources of Information** Association of Occupational and Environmental Clinics http://www.aoec.org American College of Occupational and Environmental Medicine http://www.acoem.org American College of Medical Toxicologists http://www.acmt.net American College of Preventive Medicine http://www.acpm.org ATSDR Information Center https://www.atsdr.cdc.gov/contacts.html The National Institute for Occupational Safety and Health (NIOSH) https://www.cdc.gov/niosh/hhe/ **Other CSEMs** “Case Studies in Environmental Medicine: Tetrachloroethylene Toxicity” is one monograph in a series. To view the “Taking an Exposure History” or “Taking a Pediatric Exposure History” CSEMs and other publications in this series, please go to http://www.atsdr.cdc.gov/csem/csem.html.

Key points	• Physicians should advise patients to avoid tetrachloroethylene exposures and factors that might further increase their risk for disease or worsen their existing condition(s). • Physicians should advise patients to contact them or another physician if they develop neurological problems or other health changes.
Section 3.4 **Question #1**	Patients who have been exposed to tetrachloroethylene should A. Speak to their employer about ways to reduce occupational exposure risk. B. Learn how to avoid further exposure. C. Know when to call their doctor. D. All of the above. *To review relevant content, see this entire section (3.4).*

Post-test

Instructions	Select the one best answer for each of the questions below.
Question #1	1. Which of the following statements about tetrachloroethylene is **TRUE**? A. It is well absorbed by the lungs. B. Most of an absorbed dose is metabolized in the kidney. C. Most of an absorbed dose is metabolized in the liver. D. Most of an inhaled dose is eliminated in urine.
	Answer: A Answer A is correct. The lungs absorb about 64%–100% of an inhaled tetrachloroethylene dose. About 1%–3% of the estimated amount inhaled is metabolized to trichloroacetic acid (TCA) and other chlorinated oxidation products, although additional tetrachloroethylene, as much as 20% or more of the dose, may be metabolized over a longer period. The body eliminates tetrachloroethylene via exhalation of the parent compound and urinary excretion of metabolism products. The lungs eliminate more than 70% of inhaled tetrachloroethylene unchanged. *To review relevant content, see "Biological fate of tetrachloroethylene" in Section 2.1.*
Question #2	2. The following health effects due to tetrachloroethylene toxicity are all true **EXCEPT** A. The available epidemiologic studies provide a pattern of evidence associating tetrachloroethylene exposure and several types of cancer, specifically bladder cancer and non-Hodgkin's lymphoma. B. Hepatic effects are only seen from long-term exposure. C. The IARC has classified tetrachloroethylene as "probably carcinogenic to humans." D. Neurotoxicity is the most sensitive outcome that follows either oral or inhalation exposure to tetrachloroethylene in humans.
	Answer: B All statements are true except B. Hepatotoxic effects are usually from long-tern exposure of tetrachloroethylene. However, effects such as hepatomegaly, hepatocellular damage, and elevations of gamma-glutamyltransferase and bilirubin degradation byproducts have been observed after acute high-level exposure to tetrachloroethylene. *To review relevant content, see "Clinical effects" in Section 2.2.*

Question #3	3. Which of the items listed below is a CNS effect of chronic exposure to tetrachloroethylene by inhalation? A. Paranoid psychosis. B. Dysesthesia. C. Disorientation. D. Tactile hallucinations.
	Answer: C Reported symptoms due to chronic inhalation exposure to tetrachloroethylene have included • ataxia, • disorientation, • irritability, • persistent headache, • short-term memory deficits, and • sleep disturbances. Therefore, C is correct. *To review relevant content, see "Evaluation and diagnosis" in Section 3.1.*
Question #4	4. Patients exposed to high levels of tetrachloroethylene for a short period of time might have all of the following symptoms **EXCEPT** A. Slurred speech. B. Jaundice. C. Memory deficit. D. Upper respiratory irritation.
	Answer: B All answers are correct except B. Patients exposed to high levels of tetrachloroethylene for a short period of time might have slurred speech, memory deficit, and upper respiratory irritation. Jaundice typically happens with chronic exposure. *To review relevant content, see "Evaluation and diagnosis" in Section 3.1.*
Question #5	5. An exposure history should be part of the patient history. The benefit(s) of taking an exposure history is (are) A. Making more accurate diagnoses. B. Preventing disease in others by avoiding future exposure. C. Influencing the course of disease by stopping current exposure.

	D. All of the above.
	Answer: D Answer D is correct. Taking an exposure history may enable physicians to make more accurate diagnoses, influence the course of disease by stopping current exposure, prevent disease in others by avoiding future exposure, and prompt workplace evaluations and worker protection measures. This should cover occupational and non-occupational tetrachloroethylene exposure risks. *To review relevant content, see "Evaluation and diagnosis" in Section 3.1.*
Question #6	6. The following treatment strategies for acute inhalation of tetrachloroethylene are all appropriate **EXCEPT** A. Removing from exposure, including contaminated clothing. B. Washing affected areas with mild soap and copious amounts of water. C. Providing support for respiratory and cardiovascular functions. D. Using activated charcoal.
	Answer: D All strategies are correct except D. Recommended treatment strategies include removing from exposure in all suspected cases, washing affected areas with mild soap and copious amounts of water, and administering oxygen if respiratory depression has occurred. Using charcoal and cathartics is not applicable to an inhalation exposure. *To review relevant content, see "Treatment: Acute exposure" in Section 3.2.*
Question #7	7. The following statements regarding U.S. regulations and guidelines for tetrachloroethylene are all true **EXCEPT** A. ACGIH recommends a threshold limit value of 25 ppm. B. EPA, under the Clean Air Act, regulates three types of tetrachloroethylene dry cleaners. C. The EPA will not require operators to begin reducing tetrachloroethylene emissions from dry cleaners until December 21, 2020. D. NIOSH recommends treating tetrachloroethylene in the workplace as a potential human carcinogen and reducing occupational exposure to the lowest feasible level.
	Answer: C All statements are true **EXCEPT** answer C. The three types of tetrachloroethylene dry cleaners regulated by EPA under the Clean Air Act are large industrial and commercial dry cleaners, freestanding small dry cleaners, and small dry cleaners in apartment buildings. EPA has required operators to reduce emissions from dry

	cleaners and has established a final rule on the phase out of tetrachloroethylene use in dry cleaners in residential areas by December 21, 2020. *To review relevant content, see "Regulations and guidelines" in Section 3.3.*
Question #8	8. All of the following statements about taking a patient history are correct **EXCEPT** A. An exposure history should be part of the patient medical history. B. Physicians who suspect a temporal association between symptoms and exposure to certain products should try to identify the specific chemical ingredients involved. C. An exposure history should cover both occupational and non-occupational tetrachloroethylene exposure risks. D. An exposure history gathers information about one patient only. Information regarding co-workers' activities and potential exposures is irrelevant.
	Answer: D All statements are correct **EXCEPT** answer D. The patient exposure history should gather information about potential co-worker exposure(s). *To review relevant content, see "Evaluation and diagnosis: Patient history" in Section 3.1.*
Question #9	9. Which of the following statements about exposure risk is **NOT** correct? A. People living near dry cleaning locations may be exposed to higher levels of tetrachloroethylene than the general population. B. Workers in industries such as dry cleaning, machining, and electronics have an increased likelihood of PCE exposure. C. Family members of dry-cleaning workers are not at increased risk for exposure to tetrachloroethylene. D. Tetrachloroethylene can be transmitted in breast milk, thus subjecting the nursing newborn to prolonged exposure.
	Answer: C All statements are correct except answer C. Studies have shown that the tetrachloroethylene levels in alveolar air samples were significantly higher in family members of workers than in control subjects. Higher exposures were attributed to clothing worn home from work and the expired breath of workers. *To review relevant content, see "Who is at risk for exposure to tetrachloroethylene?" in Section 1.4.*
Question #10	10. Tetrachloroethylene is

	A. A substance that has low vapor pressures at room temperature. B. A clear synthetic liquid that is easily dissolved in water. C. Widely used for dry cleaning fabrics and for metal degreasing operations and in some consumer products. D. All of the above.
	Answer: C Answer C is correct. Tetrachloroethylene is a synthetic chemical. It is a clear, colorless, nonflammable liquid with a sweet, fruity odor and a low aqueous solubility. It is volatile and readily evaporates at room temperature. It is widely used for dry cleaning fabrics and for metal degreasing operations and in some consumer products. *To review relevant content, see "What is tetrachloroethylene?" in Section 1.1.*
Question #11	11. Which of the following statements regarding sources of tetrachloroethylene is **NOT** correct? A. Ambient air concentrations of tetrachloroethylene vary from source to source and with distance from the source. B. In areas near sources of contamination, ground water and surface water concentrations can be considerably higher than in areas at a distance from sources of contamination. C. Occupational exposure of tetrachloroethylene has been decreasing over the past several decades. D. Tetrachloroethylene breaks down quickly in the environment.
	Answer: D All statements are correct except answer D. Tetrachloroethylene breaks down very slowly in the environment. It has relatively low solubility in water and has medium-to-high mobility in soil; thus, its residence time in surface environments is not expected to be more than a few days. However, it persists in the atmosphere for several months and can last for decades in the groundwater. It can migrate through groundwater (or soil) up into the air of homes and buildings through vapor intrusion. *To review relevant content, see "Where is tetrachloroethylene found?" in Section 1.2.*
Question #12	12. Which of the following tetrachloroethylene exposure route(s) is (are) common in the general population? Select the best answer. A. Inhalation. B. Ingestion. C. Skin. D. Inhalation + Ingestion.

	Answer: D The best answer is D. The primary routes of exposure to tetrachloroethylene for the general population are inhalation, including vapor intrusion from contaminated soil and water, and swallowing contaminated water. *To review relevant content, see "What are the primary routes of exposure to tetrachloroethylene?" in Section 1.3.*
Question #13	13. Which of the following steps in counseling patients have the best answer? A. Advise patients to avoid exposures and conditions that might further increase their risk for disease or worsen their existing conditions. B. Advise patients to consult you or another physician if they develop signs or symptoms of CNS disorders and other health effects, especially those possibly related to liver or kidney problems. C. Consult with a specialist in occupational and environmental medicine or others with expertise and experience treating patients exposed to tetrachloroethylene to develop a periodic monitoring plan, as appropriate. D. All of the above.
	Answer: D Answers A-C are all correct. Therefore answer D is the best choice. *To review relevant content, see "Counseling and prevention" in Section 3.4.*
Question #14	14. Which of the following indicator(s) confirm(s) tetrachloroethylene exposure? A. Trichloroacetic acid in blood or urine. B. Tetrachloroethylene in breath, blood, or urine. C. Elevated values of renal and liver function tests. D. Hepatic ultrasound.
	Answer: B Answers A, C, and D are all non-specific to tetrachloroethylene exposure. Answer B is correct. Tetrachloroethylene may be measured in breath, blood, or urine to confirm the exposure. However, these laboratory studies are not rapidly available and do not change management priorities. Thus the diagnosis of hydrocarbon exposure is based upon clinical features. *To review relevant content, see "Direct biologic indicators" in Section 3.1.*

Relevant Content

Question	
1.	Section 2.1 Biological fate of tetrachloroethylene • Explain the major pathways of tetrachloroethylene in the body (learning objective)
2.	Section 2.2 Clinical Effects • Describe the clinical effects associated with tetrachloroethylene exposure
3.	Section 3.1 Evaluation and diagnosis • Describe possible clinical symptoms in patients exposed to tetrachloroethylene,
4.	Section 3.1 Evaluation and diagnosis • Describe possible clinical symptoms in patients exposed to tetrachloroethylene
5.	Section 3.1 Evaluation and diagnosis • Describe what is included in the initial history of patients potentially exposed to tetrachloroethylene
6.	Section 3.2 Treatment • Describe treatment strategies for patient with tetrachloroethylene poisoning
7.	Section 3.3 Regulations and guidelines • Identify existing standards and guidelines for tetrachloroethylene in the workplace
8.	Section 3.1 Evaluation and diagnosis • Describe what is included in the initial history of patients potentially exposed to tetrachloroethylene • Describe what is included in the physical examination of patients potentially exposed to tetrachloroethylene • Identify tests that can help diagnose tetrachloroethylene toxicity
9.	Section 1.4 Risk for Exposure • Identify the populations with potentially high exposures to tetrachloroethylene

10.	Section 1.1 What is • Describe uses of tetrachloroethylene
11.	Section 1.2 Where found • Identify sources of tetrachloroethylene exposure.
12.	Section 1.3 Primary routes of exposure • Describe how people are exposed to tetrachloroethylene.
13.	Section 3.4 Counseling and prevention • Identify suitable self-care for patients exposed to tetrachloroethylene, • Identify clinical follow-up for patients exposed to tetrachloroethylene, and • Describe how to counsel patients appropriately on how to avoid further exposure to tetrachloroethylene.
14.	Section 3.1 Direct biologic indicators • Identify tests that can help diagnose tetrachloroethylene toxicity.

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