

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

[Trichloroethylene Toxicity](#)

Course: SS4561

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Background

Course Overview

<p>Course overview</p>	<p>This Case Study in Environmental Medicine (CSEM) provides an overview of trichloroethylene toxicity. Trichloroethylene is widely used for vapor degreasing of fabricated metal parts in the automotive and metal industries and has some limited uses in consumer and commercial products. Knowledge from this course will help health care providers diagnose and treat patients exposed to trichloroethylene.</p> <p>This online course will take about approximately 150 minutes to complete. You may finish the entire CSEM in one session or complete each chapter separately.</p> <p>The course begins with a patient case study to help you assess your current knowledge about trichloroethylene toxicity.</p>
<p>Course learning objectives</p>	<p>After completing this course, you will be able to</p> <ul style="list-style-type: none"> • Describe the latest science on TCE exposure in both environmental and occupational settings. • Discuss potential adverse clinical effects associated with TCE exposure. • Describe how to clinically manage patients exposed to TCE. • Describe how to improve collaborative practice across the healthcare team regarding the diagnosis and treatment of patients exposed to TCE.
<p>Key concepts</p>	<p>Key concepts in this course include</p> <ol style="list-style-type: none"> 1. Trichloroethylene (TCE) is a common industrial solvent and contaminant of hazardous waste sites, groundwater, and drinking water. 2. TCE poses a potential human health hazard for noncancer toxicity to the central nervous system, kidney, liver, immune system, male reproductive system, and the developing embryo/fetus. 3. The National Toxicology Program and the U.S. Environmental Protection Agency (EPA) concludes that TCE is characterized as “carcinogenic to humans” by all routes of exposure. 4. Symptoms and signs potentially associated with TCE exposure are nonspecific, making a careful medical and exposure history essential to diagnosis. 5. There is no antidote for TCE poisoning.

CSEM overview	<p>The goals of the CSEM series are to</p> <ul style="list-style-type: none"> • increase the primary care provider’s knowledge of hazardous substances in the environment and • help clinicians evaluate and treat potentially exposed patients.
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Pre-course Knowledge Check

Introduction	This case study will help you assess your pre-course knowledge about trichloroethylene toxicity. Read the case presentation and answer the questions that follow.
Case presentation	<p>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.</p> <p>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). 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 says he is familiar with TCE; it is used in the electronics plant where he works.</p> <p>The daughter, aged 4 years, had several ear infections during her first 2 years, culminating in a myringotomy at age 3 years. Follow-up by an ear, nose, and throat 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.</p> <p>The mother, aged 33 years, then reveals that she might 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 fetus was likely to be "damaged." They are also concerned that the entire family might suffer from cancer or other diseases in the future.</p> <p>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 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 drinks is two to three glasses a day.</p> <p>You schedule each parent and the child for an individual office visit.</p>

Knowledge check	
Question #1	<p>What would you include in the mother's and daughter's problem list?</p> <p>Answer: The mother has a focused concern about the effects of exposure; the child has frequent otitis media (status post myringotomy and tympanostomy tube placement) and frequent upper respiratory infections.</p> <ul style="list-style-type: none"> • The Case Presentation in the Pre-course Knowledge Check covers this information.
Question #2	<p>What additional information would you seek before seeing the family again?</p> <p>Answer: You will need</p> <ul style="list-style-type: none"> • information on TCE toxicity, including reproductive and developmental effects. • information on TCE contamination of the family's drinking water, including duration and level of contamination; and • copies of information provided to the family by the municipal water company and responses, if any, from local and state health agencies. <p>When appropriate, consult a specialist in occupational and environmental medicine.</p> <ul style="list-style-type: none"> • Chapter 1, Section 1.3 and Chapter 2, Section 2.2 cover this information.
Question #3	<p>What reassurances might you provide at the end of this initial visit?</p> <p>Answer: None of the symptoms described in the case indicate serious illness. However, you should reassure the family that you will perform a complete physical examination 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 might not be appropriate. You might indicate that you will consult sources of information on TCE's effects on pregnancy. It is important to maintain a balance between reassurance 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 might develop an illness, including cancer.</p>

	<ul style="list-style-type: none"> Chapter 2, Section 2.2 and Chapter 3, Section 3.1 cover this information.
Question #4	<p>What are the possible sources of exposure to TCE for the family described in the case study?</p> <p>Answer: Possible sources of the family's TCE exposure include home drinking water (ingestion and dermal and inhalation exposure during bathing), the father's workplace (inhalation and possibly dermal), and the daughter's day-care center (inhalation). Exposure also might occur from washing dishes, laundry, cooking, or any other use of hot water in the home, or use of TCE-containing consumer products such as correction fluid or spot removers.</p> <ul style="list-style-type: none"> Chapter 1, Section 1.2 covers this information.
Question #5	<p>Which members of the family described in the case study are at increased risk for adverse effects from TCE? Explain.</p> <p>Answer: All members of the family described in the case study might be at increased risk for adverse effects from overexposure to TCE.</p> <ul style="list-style-type: none"> Chapter 1, Section 1.4 covers this information.
Question #6	<p>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 TCE exposure. What biologic indicators of TCE exposure are likely being measured?</p> <p>Answer: The most convenient biologic indicators of TCE exposure are the urinary metabolites, trichloroethanol and trichloroacetic acid. However, these metabolites are not specific to TCE because they are also metabolites of tetrachloroethylene (perchloroethylene), 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.</p> <ul style="list-style-type: none"> Chapter 3, Section 3.1 covers this information.
Question #7	<p>If biologic measurements are performed, what considerations should be taken into account to properly interpret the results?</p> <p>Answer: To properly interpret any of the tests mentioned in answer 6, knowledge of the time lapse between exposure and collection is needed. To prevent contamination or sample loss (evaporation or adsorption), proper collection,</p>

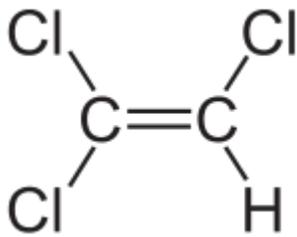
	<p>handling, storage, and transportation procedures must be followed. Members of this family likely would have elevated levels of TCE or its metabolites above background levels for a few hours after exposure, for instance, after they shower. However, there are no appropriate reference values currently available for a health risk assessment.</p> <ul style="list-style-type: none"> Chapter 3, Section 3.1 covers this information.
Question #8	<p>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?</p> <p>Answer: No further studies are indicated for TCE exposure. A workup for fatigue can indicate additional tests.</p>
Question #9	<p>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 further evaluation is indicated. What is your response?</p> <p>Answer: Evidence from animal and epidemiologic studies suggests that several reproductive and developmental toxicity end points might be associated with TCE exposure, including infertility in males and females, impaired fetal growth, and cardiac teratogenesis. Additional evaluation with fetal echocardiogram is therefore justified in this case. Depending on findings, it may be helpful to consult a maternal fetal medicine specialist for additional recommendations.</p> <ul style="list-style-type: none"> Chapter 2, Section 2.2 covers this information.
Question #10	<p>You evaluate the 4-year-old child. A review of her history reveals three to four episodes of otitis media, which were treated with ampicillin, in each of the last 3 years. 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. You referred her to an otolaryngologist, who performed a myringotomy and tympanostomy without incident. The mother estimates the child had four episodes of coryza or mild influenza last year, with about 7 days of illness that merited staying home from day care.</p> <p>Does this pattern reflect compromise of the child's immune system?</p> <p>Answer: No. A survey of infections in children younger than 3 years 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). More than 3% of the children in day care were hospitalized for tympanostomies</p>

	(Bell et al., 1989). 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.
Question #11	<p>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?</p> <p>Answer: No. Immunocompetence tests are not appropriate because no evidence of immune function abnormalities has been found in this case.</p> <p>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.</p> <ul style="list-style-type: none"> • Chapter 3, Section 3.1 Covers this information.
Question #12	<p>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?</p> <p>Answer: The EPA has identified TCE as one of 33 hazardous air pollutants that present the greatest threat to public health in urban areas. Per EPA's National Ambient Air Quality Standards in the Clean Air Act, TCE is controlled as a volatile organic compound under state regulations implementing the standards for ozone.</p> <p>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 state agency responsible for enforcement of air standards should be contacted to investigate possible release of TCE onto the day-care center property.</p> <ul style="list-style-type: none"> • Chapter 3, Section 3.3 covers this information.

CHAPTER 1. EXPOSURE BASICS

Contents	<p>Chapter 1 will cover the following topics:</p> <ol style="list-style-type: none"> 1. What is trichloroethylene? 2. Where is trichloroethylene found? 3. What are the primary routes of exposure to trichloroethylene? 4. Who is at risk for exposure to trichloroethylene?
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Section 1.1. What Is Trichloroethylene?

Learning objective 1	<p>After completing this section, you will be able to</p> <ul style="list-style-type: none"> • define TCE properties.
Properties	<ul style="list-style-type: none"> • Trichloroethylene (TCE) (C₂HCl₃) is a synthetic chemical. • TCE is a clear, colorless, nonflammable liquid with a sweet, fruity odor. • TCE is a lipophilic, volatile organic compound, and readily evaporates at room temperature. • TCE is slightly soluble in water; soluble in ethanol, acetone, diethyl ether, and chloroform; and miscible in oil. <div style="text-align: center;">  </div>
Use	<p>Historically, TCE had a wide range of uses, including intermediate chemicals, industrial and commercial solvents, pharmaceuticals, insecticides, fumigants, textiles, adhesives, and paints. However, as of 2011, most U.S. consumption (EPA, 2014) is attributable to two specific uses:</p> <ul style="list-style-type: none"> • As an intermediate chemical in a closed system for manufacturing refrigerant chemicals – 83.6% • As a solvent for vapor degreasing of metal parts – 14.7%

	<ul style="list-style-type: none"> • Other uses, including as a spot-removal agent in the dry-cleaning industry, and in certain consumer products (spray fixatives for arts and craft uses) – 1.7%
Environmental fate	<p>In the atmosphere, TCE is destroyed by photooxidation, with a half-life of 3–8 days during the summer months and approximately 2 weeks in cold climates during the winter. 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.</p> <p>TCE volatilizes quickly from water at a rate that depends on temperature, water movement, and aeration. The biodegradation of TCE under anaerobic conditions is slow, making TCE relatively persistent in subsurface waters, with a half-life of months to years.</p>
Synonyms	<p>Trichloroethylene is also known as</p> <ul style="list-style-type: none"> • TCE, • 1,1,2-trichloroethene, • acetylene trichloride, and • Trichloroethene
Key point	<ul style="list-style-type: none"> • TCE is a synthetic chemical that is now mainly used as a chemical intermediate and a metal degreaser. • TCE is used in certain consumer products.
Section 1.1 Question #1	<p>All of the following statements about TCE are correct EXCEPT:</p> <ol style="list-style-type: none"> TCE is a synthetic chemical mainly used for producing other chemicals and metal degreasing. TCE is a volatile organic compound that readily evaporates at room temperature. TCE is used in certain consumer products. The main use of TCE is in the vapor degreasing of metal parts. <p>Answer: D</p> <p>This statement is not true anymore. Recent data show that most U.S. consumption of TCE is attributable to two specific uses: 83.6% of total TCE production volume is used as an intermediate for manufacturing refrigerant chemicals, and 14.7% is used as a solvent for metal degreasing; the remaining 1.7% is attributed to other uses.</p> <p>To review relevant content, see “Properties” and “Use” in Section 1.1.</p>

Section 1.2. Where Is Trichloroethylene Found?

Learning objective 1 (cont.)	<p>After completing this section, you will be able to</p> <ul style="list-style-type: none"> • define sources of TCE exposure.
Overview	<p>Numerous people living in the United States are or have been exposed to TCE because of its widespread presence from past and current uses. In addition to occupational exposure of workers in industries using TCE, the general population can be exposed to TCE in ambient air, drinking water supplies, certain consumer products, and contaminated foods (ATSDR, 2019; EPA, 2011c; NTP, 2016).</p> <p>In general, atmospheric levels are highest in areas of concentrated industry and population and lower in rural and remote regions. Mean TCE concentrations measured in air at locations across the United States are generally between 0.01 ppb and 0.3 ppb, although mean levels as high as 3.4 ppb have been reported (EPA 2011a).</p> <p>Workers, particularly in the degreasing industry, are exposed by inhalation to the highest levels of TCE. Based on monitoring surveys, these workers might be exposed to levels ranging from approximately 1 ppm to 100 ppm.</p> <p>The general population can also be exposed to TCE by contact with or consumption of water from supplies contaminated with the chemical, by consumption of contaminated foods, and by contact with consumer products containing the compound.</p> <p>Between 4.5% and 18% of the drinking water supply sources in the United States that are tested on a yearly basis by EPA have some TCE contamination. Levels are typically <30 ppb. TCE levels in the low parts per billion range have been measured in food; however, levels as high as 140 ppb were measured in a few samples. Note that the amount of TCE found by chemical analysis is not necessarily the amount that is bioavailable (ATSDR 2019).</p>
Occupational sources	<p>Occupational exposures can occur in chemical industries that manufacture</p> <ul style="list-style-type: none"> • pentachloroethane, • polyvinyl chloride, and • other polychlorinated aliphatic hydrocarbons, flame retardant chemicals, and insecticides where TCE is a chemical intermediate. <p>Other potential exposures occur in the manufacturing processes of</p>

	<ul style="list-style-type: none"> • disinfectants • dyes • perfumes • pharmaceuticals • soaps <p>The following occupations also have increased likelihood of exposure</p> <ul style="list-style-type: none"> • dry cleaners • mechanics • oil processors • printers • resin workers • rubber cementers • shoemakers • textile and fabric cleaners • varnish workers • workers reducing nicotine in tobacco
<p>Environmental sources</p>	<p>TCE can be released to air, water, and soil at places where it is produced or used.</p> <p>Air</p> <p>TCE is widely detected in ambient air. EPA reports the annual mean concentrations of TCE measured at approximately 300 locations across the United States between 1998 and 2008. Annual mean TCE concentrations at most of these locations were between 0.01 ppb and 0.3 ppb. Some locations had annual mean levels as high as 0.7–3.4 ppb (ATSDR, 2019; EPA, 2011a).</p> <p>Water</p> <p>TCE is a common groundwater and drinking water contaminant. TCE has been detected in many samples taken from drinking water supplied by contaminated sources from which TCE and other volatile organic compounds are not always completely removed by conventional water treatment. EPA (EPA, 2011b) conducts yearly monitoring of the concentrations of TCE in public water systems located across the United States. During 2005, TCE was detected in 2,292 out of 46,937 samples (4.9%) collected from groundwater-supplied systems and 1,874 out of 12,705 samples (14.8%) collected from surface-water supplied systems (ATSDR, 2019).</p>

	<p>Because of TCE's volatility, household activities such as bathing, laundering, and cooking with contaminated water can produce TCE air concentrations above ambient levels.</p> <p>Food</p> <p>Natural and processed foods can 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. TCE was detected in 30 table-ready food items collected from supermarkets across the United States during a 5-year study (1996–2000) conducted by the U.S. Food and Drug Administration (FDA) (Fleming-Jones ME, 2003).</p> <p>Soil</p> <p>TCE can be released into the soil through industrial discharges into surface waters and through landfill leachate (ATSDR, 2019).</p>
<p>Sources from consumer products</p>	<p>TCE has been listed as a major ingredient in several consumer products, such as</p> <ul style="list-style-type: none"> • degreasers intended for use in automotive products, • adhesives, • cleaning fluids for rugs, • paint removers/strippers, • spot removers, and • typewriter correction fluids.
<p>Key point</p>	<ul style="list-style-type: none"> • Numerous people living in the United States have been or are being exposed to TCE because of its widespread presence from past and current uses.
<p>Section 1.2</p> <p>Question #1</p>	<p>TCE has become a common environmental contaminant. What sources does contamination result from?</p> <p>A. Evaporative losses during use B. Discharge to surface waters and groundwater by industry, commerce, and individual consumers C. Leaching from hazardous waste landfills into groundwater D. All of the above</p> <p>Answer: D</p> <p>Because of its widespread use, TCE has become a common environmental contaminant. Contamination results from evaporative losses during use;</p>

	<p>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.</p>
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	<p>To review relevant content, see “Environmental sources” in Section 1.2.</p>
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Section 1.3. What are the primary routes of exposure to trichloroethylene?

Learning objective 2	<p>After completing this section, you will be able to</p> <ul style="list-style-type: none"> describe routes of exposure.
Overview	<p>Occupational exposure to TCE can occur through inhalation and skin contact at workplaces where TCE is produced or used.</p> <p>The general population might be exposed to TCE via inhalation of indoor and outdoor air, ingestion of food and or contaminated drinking water, or dermal exposure to contaminated water.</p>
Inhalation	<p>Inhalation is the primary route of exposure to TCE, as a result of TCE's volatility. Inhalation is the route that most commonly leads to acute illness. Some exposure scenarios in which TCE-contaminated air might be inhaled include the following:</p> <ul style="list-style-type: none"> Bathing and other household water uses, such as dishwashing, clothes washing, and toilet use, through release of vapors Accidental spills, and use of TCE-containing products in small, enclosed spaces Deliberate abuse (e.g., TCE-induced euphoria) Working in the same space as others who are using TCE Work and hobby activities involving TCE and TCE-containing products Spending time in areas where TCE is released to air and water by evaporation or fugitive emissions from industrial activities and from landfills From worker's skin and clothing
Ingestion	<p>Ingestion is typically a minor pathway of exposure because TCE is not normally present at high levels in food or water. Ingestion of TCE might occur through</p> <ul style="list-style-type: none"> incidental addition of TCE during food production swallowing food or drinking water contaminated with TCE
Dermal	<p>Skin contact is a common route of TCE exposure in the workplace and among the general public if they are bathing in TCE-contaminated water. Skin contact is less important in a clinical setting because it is not likely to cause toxic effects under normal conditions. It might, however, contribute to overall exposure and chronic risk.</p>
Key point	<ul style="list-style-type: none"> Inhalation is the primary route of exposure to TCE and the route that most commonly leads to acute illness.

Section 1.3: Question #1	<p>The primary route of exposure to trichloroethylene is</p> <ul style="list-style-type: none">A. IngestionB. InhalationC. Dermal contactD. All are equally important <p>Answer: B</p> <p>Inhalation is the primary route of exposure to trichloroethylene, and the route that most commonly leads to acute illness.</p> <p>To review relevant content, see “Inhalation” in Section 1.3.</p>
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Section 1.4. Who is at risk for exposure to trichloroethylene?

Learning objective 2 (cont.)	<p>After completing this section, you will be able to</p> <ul style="list-style-type: none"> • identify the populations with potentially high exposures to trichloroethylene.
Overview	<p>The Environmental Protection Agency (EPA) recently finalized its risk assessment of TCE, which identified health risks to</p> <ul style="list-style-type: none"> • workers when TCE is used as a degreaser in small commercial shops and as a stain removing agent in dry cleaning • consumers who use spray aerosol degreasers and spray fixatives
General Populations	<p>The general population can be exposed to TCE via inhalation of ambient air, ingestion of food and drinking water contaminated with TCE, or skin contact with TCE contaminated water. Water and air become contaminated by releases of TCE from active industries or from hazardous waste sites. A survey conducted by the National Health and Nutrition Examination Survey (NHANES) from 1988 to 1994 tested 677 whole-blood samples for TCE. The results suggested that approximately 10% of the U.S. population had detectable levels of TCE in their blood. More recently, NHANES tested 3,178 samples from 2005–2006 and 2,952 samples from 2007–2008. Those results detected TCE in the blood of less than 5% of people in all age groups, genders, and races or ethnicities studied in the surveys (CDC, 2011, 2016).</p>
Workers	<p>An estimated 300,000 workers are exposed in dry cleaning facilities that use TCE to remove spots from garments before or after dry cleaning. An estimated 30,000 additional workers are potentially exposed to TCE at small commercial degreasing operations (EPA 2014; NTP 2016).</p> <p>The Occupational Safety and Health Administration (OSHA) Chemical Exposure Health Database (which includes results for 3,600 air samples from 1984 to 2011) reported that from 2000 to 2010, 92 samples exceeded the OSHA permissible exposure limit of 100 ppm. Among those samples, two exceeded the National Institute for Occupational Safety and Health “immediately dangerous to life or health” level of 1,000 ppm (NTP 2016).</p>
Consumers	<p>An EPA risk assessment (EPA, 2014) reported that TCE constituted 80% to 100% of three aerosol spray fixative products for arts and crafts uses and other products intended for use as cleaners or degreasers in automobile or home maintenance. However, EPA was not able to estimate the numbers of consumers or bystanders exposed to TCE from arts and crafts spray products or degreasers (NTP, 2016).</p>

Others	Because TCE can cross the placenta as well as accumulate in breast tissue, the fetus and nursing newborn of women at risk for exposure might be exposed to TCE.
Key points	<ul style="list-style-type: none"> • The general population can be exposed to TCE by inhaling contaminated air, eating food and drinking water contaminated with TCE, or skin contact with TCE-contaminated water. • A recent NHANES survey shows an overall decrease in TCE exposure in the general population. • Workers in metal-degreasing and dry-cleaning operations have the greatest likelihood of exposure to high concentrations of TCE. • The numbers of consumers exposed to TCE are not known.
Section 1.3: Question #1	<p>Of the following, which statement about TCE exposure risk is NOT correct?</p> <p>A. The general population is exposed to TCE primarily by drinking contaminated water and inhaling contaminated indoor air.</p> <p>B. Recent data show an overall increase in TCE exposure in the general population.</p> <p>C. Workers in metal-degreasing and dry-cleaning operations have the greatest likelihood of exposure to high concentrations of TCE.</p> <p>D. Unknown numbers of consumers are exposed to TCE from aerosol spray fixative products for arts and crafts uses and other products intended for use as cleaners or degreasers in automobile or home maintenance.</p> <p>Answer: B</p> <p>The statement B is not correct. Recent NHANES survey shows an overall decrease in TCE exposure in the general population. The other three statements are correct.</p> <p>To review relevant content, see Section 1.4.</p>

CHAPTER 2. BIOLOGICAL AND CLINICAL EFFECTS OF TRICHLOROETHYLENE EXPOSURE

Contents	<p>Chapter 2 will cover the following topics:</p> <p>Section 2.1. Biological fate of trichloroethylene</p> <p>Section 2.2. Clinical effects</p>
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Section 2.1. Biological fate of trichloroethylene

Learning objective 3	<p>After completing this section, you will be able to</p> <ul style="list-style-type: none"> • explain the major pathways of TCE metabolism in the body.
Overview	<p>TCE is readily absorbed into the bloodstream, regardless of the route of exposure, and rapidly distributed throughout the body via the circulatory system. Metabolism of TCE in the kidneys and liver plays a key role in TCE toxicity. The majority of TCE absorbed into the body is eliminated by metabolism.</p>
Absorption and distribution	<p>TCE is a lipophilic, volatile compound that is readily absorbed from inhaled air. Uptake from inhalation is rapid. The absorbed dose is proportional to the exposure concentration and duration and pulmonary ventilation rate. Available reports on human exposure to TCE via ingestion are largely restricted to case reports of occupational or intentional (suicidal) ingestions and suggest significant gastric absorption. Absorption through the skin has been shown to be rapid after vapor and liquid TCE contact with the skin (EPA, 2011c).</p> <p>Several studies of tissue distribution in humans after inhalation exposure to TCE reported that the relative proportions varied among individuals, but the major sites of distribution appeared to be body fat and the liver. (ATSDR, 2019).</p>
Metabolism and role of metabolism in TCE toxicity	<p>TCE undergoes metabolism by two distinct pathways:</p> <ul style="list-style-type: none"> • CYP-oxidation by a cytochrome P450 enzyme • GSH-conjugation by the compound glutathione <p>These two metabolic pathways usually modify substances that enter the body to make them less toxic and more likely to be eliminated by excretion. However, in some cases (as with TCE), the chemical modifications can instead make the substance more toxic (NTP, 2016).</p> <p>The mutagenic and carcinogenic potential of TCE is generally thought to</p>

	<p>result from reactive intermediate biotransformation products rather than TCE itself.</p> <p>The CYP-oxidation-derived metabolites of TCE that have been associated with specific target organs, such as the liver and lungs, include the following:</p> <ul style="list-style-type: none"> • chloral hydrate • trichloroacetic acid (TCA) • dichloroacetic acid <p>The GSH-conjugation-derived metabolites of TCE that have been associated with the kidney as a target organ include the following:</p> <ul style="list-style-type: none"> • dichlorovinyl glutathione • dichlorovinyl cysteine (DCVC) <p>The majority of TCE absorbed into the body is eliminated by metabolism. Kidney cancer most likely occurs as a result of GSH conjugation of TCE, whereas liver cancer most likely occurs as a result of the CYP-oxidation pathway (Chiu et al., 2013; EPA, 2011c; NTP, 2016; Rusyn et al., 2014).</p>
Elimination	<p>Although a small amount of absorbed TCE is exhaled unchanged, most of an absorbed dose is metabolized in the body. With the exception of carbon dioxide, which is eliminated solely via exhalation, most TCE metabolites have low volatility and, therefore, are excreted primarily in urine and feces (EPA, 2011c).</p> <p>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 (Monster, Boersma, & Duba, 1979; Sato, Nakajima, Fujiwara, & Murayama, 1977).</p>
Key points	<ul style="list-style-type: none"> • TCE is readily absorbed into the bloodstream regardless of the route of exposure. • The majority of TCE absorbed into the body is eliminated after metabolism through the urine and feces. • The mutagenic and carcinogenic potential of TCE is the result of TCE metabolites rather than TCE itself.
Section 2.1: Question #1	All of the following statements about biological fate of TCE are correct EXCEPT

- A. A small amount is exhaled unchanged.
- B. Most of the absorbed dose is metabolized.
- C. The toxicity of TCE is reduced after metabolism.
- D. The metabolites of TCE are detectable in urine for a week.

Answer: C

All of the statements about biological fate of TCE are correct, except answer C. TCE becomes more toxic after it is metabolized in the kidneys and liver. The mutagenic and carcinogenic potential of TCE is generally thought to result from reactive intermediate biotransformation products rather than TCE itself.

To review relevant content, see all contents in Section 2.1.

Section 2.2. Clinical effects

Learning objective 3 (cont.)	<p>After completing this section, you will be able to</p> <ul style="list-style-type: none"> • explain potential health effects of exposure to elevated levels of TCE.
Overview	<p>TCE is carcinogenic to humans by all routes of exposure and poses a potential human health hazard for noncancer toxicity to the nervous system, kidneys, liver, immune system, male reproductive system, and the developing embryo/fetus. These conclusions are based on analyses of a broad spectrum of information from thousands of scientific studies and input from numerous scientific reviews (Chiu et al., 2013).</p>
Susceptibility and dose-response	<p>As TCE toxicity and carcinogenicity are generally associated with TCE metabolism, susceptibility to TCE health effects might be modulated by factors affecting toxicokinetics, including lifestage, gender, genetic polymorphisms, race/ethnicity, preexisting health status, lifestyle, and nutrition status. Although some of these factors are known risk factors for effects associated with TCE exposure, but how TCE interacts with known risk factors for human diseases is not known.</p> <p>An underlying assumption in deriving reference values for noncancer effects is that the dose-response relationship for these effects has a threshold. For some effects, a practical threshold (i.e., a threshold within the range of environmental exposure levels of regulatory concern) might not exist (EPA, 2011c). This is particularly true for effects on very sensitive processes (e.g., developmental processes) or effects for which there is a nontrivial background level and even small exposures might contribute to background disease processes in more susceptible people.</p>
Neurological effects	<p>Human and animal studies have associated TCE exposure with effects on several neurological domains (Chiu et al., 2013; EPA, 2011c).</p> <p><u>Strong evidence</u>, based on multiple human and experimental animal studies, shows that TCE might cause</p> <ul style="list-style-type: none"> • Changes in trigeminal nerve function or morphology • Impairment of vestibular function <p><u>Limited evidence</u>, primarily from experimental animal studies, with fewer or more-limited human studies, shows that TCE might cause</p> <ul style="list-style-type: none"> • Delayed motor function, including during neurodevelopment • Changes in auditory, visual, and cognitive function or performance
Hepatic effects	<p><i>Non-cancer toxicity</i></p> <p><u>Limited evidence</u> in humans and <u>strong evidence</u> from experimental</p>

	<p>animal studies show that, at effect levels, TCE causes hepatotoxicity but not necrosis.</p> <p>Mice appear to be more sensitive than other experimental species, and hepatotoxicity is likely mediated through oxidative metabolites including, but not exclusively, TCA.</p> <p>The hepatotoxicity shown in laboratory animals includes increased liver weight, small transient increases in DNA synthesis, cytomegaly in the form of swollen or enlarged hepatocytes, increased nuclear size (probably reflecting polyploidization), and proliferation of peroxisomes (EPA, 2011c).</p> <p><i>Cancer toxicity</i></p> <p><u>Limited evidence suggests liver carcinogenicity</u> in humans. Positive associations have been observed in some cohort studies. However, there were few cases of liver cancer among study participants, which limits the ability to determine exposure-response relationships and causality. A consistent hepatocarcinogenic response has been observed using mice of differing strains and genders and from differing routes of exposure, although some studies were confounded by various limitations (Chiu et al., 2013; EPA, 2011c).</p>
Renal effects	<p><i>Non-cancer toxicity</i></p> <p><u>Strong evidence</u> indicates that TCE might cause nephrotoxicity, particularly by damaging renal tubules. This is based on mechanistic studies, animal experiments, and a few human studies. Kidney damage is likely mediated by S-(1,2-dichlorovinyl)-L-cysteine (DCVC), a metabolite of TCE formed via glutathione conjugation and further enzyme activity (Chiu et al., 2013).</p> <p><i>Cancer toxicity</i></p> <p><u>Strong evidence</u> shows a causal association between TCE exposure and kidney cancer in humans across 15 independent epidemiologic studies of different study designs and populations from different countries. Convincing evidence from animal studies provided further biological plausibility for the epidemiologic findings of TCE-induced kidney cancer. (EPA, 2011c; Fevotte et al., 2006; Moore et al., 2010; Scott & Jinot, 2011).</p>
Developmental effects	<p><u>Strong evidence</u>, based on multiple human and animal studies, shows that TCE might cause fetal cardiac malformations.</p>

	<p><u>Limited evidence</u>, primarily from experimental animal studies, with limited epidemiologic studies, indicates that TCE might cause other fetal malformations (in addition to cardiac), prenatal losses, decreased growth or birth weight of offspring, and alterations in immune system function (Chiu et al., 2013; EPA, 2011c).</p>
Reproductive effects	<p><u>Strong evidence</u>, based on multiple human and experimental animal studies, shows that TCE might cause male reproductive toxicity, primarily through effects on the testes, epididymides, sperm, or hormone levels.</p> <p><u>Limited evidence</u>, based on few and limited human and experimental animal studies, indicates that TCE might cause female reproductive toxicity (Chiu et al., 2013; EPA, 2011c).</p>
Immune system effects	<p><u>Strong evidence</u>, based on multiple human and experimental animal studies, shows that TCE exposure might cause autoimmune disease, including scleroderma, and a specific type of generalized hypersensitivity disorder.</p> <p><u>Limited evidence</u>, primarily from experimental animal studies, with fewer or more limited human studies, indicates that TCE might cause immunosuppression (Chiu et al., 2013; EPA, 2011c).</p>
Carcinogenic effects	<p>EPA conducted a systematic review of 76 human epidemiologic studies on TCE and cancer (EPA, 2011c; Scott & Jinot, 2011). A meta-analysis of these studies was conducted for liver cancer, kidney cancer, and non-Hodgkin lymphoma.</p> <p>A summary of the weight of evidence on consistency of the observed association between TCE exposure and cancer follows (Chiu et al., 2013; EPA, 2011c):</p> <p><u>Strong evidence</u> of consistency for kidney cancer (consistently elevated relative risks [RR]). Meta-analysis yielded robust, statistically significant summary RR, with no evidence of heterogeneity or potential publication bias.</p> <p><u>Moderate evidence</u> of consistency for non-Hodgkin lymphoma (consistently elevated RR): RR estimates more variable compared with kidney cancer. Meta-analysis yielded robust, statistically significant summary RR, with some heterogeneity (not statistically significant) and some evidence for potential publication bias.</p> <p><u>Limited evidence</u> of consistency for liver cancer (fewer studies overall, more variable results): Meta-analysis showed no evidence of heterogeneity or potential publication bias.</p>

	Supported by the analyses described above and following the EPA's Guidelines for Carcinogen Risk Assessment (U. S. EPA, 2005), EPA concludes that TCE is characterized as "carcinogenic to humans" by all routes of exposure (EPA, 2011c). The International Agency for Research on Cancer has concluded that TCE is carcinogenic to humans (Group 1) (IARC, 2018). The U.S. Department of Health and Human Services considers TCE to be a known human carcinogen (NTP, 2016).
Other clinical effects	<p>Respiratory: Suggestive evidence, primarily from short-term experimental animal studies, shows that TCE might cause respiratory tract toxicity, primarily in Clara cells, and pulmonary tumors in mice only (Chiu et al., 2013).</p> <p>Skin: Like other organic solvents, TCE can produce contact dermatitis, rashes, and burns. The defatting dermatitis resulting from prolonged contact might reduce resistance to skin infections (ATSDR, 2019; EPA, 2011c).</p>
Key points	<ul style="list-style-type: none"> • Strong evidence shows that TCE is a potential human health hazard to the nervous system, kidneys, liver, immune system, male reproductive system, and the developing embryo/fetus. • TCE is carcinogenic to humans by all routes of exposure. • Even small exposures might contribute to disease processes in more susceptible people.
Section 2.2: Question #1	<p>EPA's conclusion concerning TCE carcinogenicity was primarily based on strong evidence of consistently elevated relative risks between TCE exposure and WHAT cancer in humans?</p> <p>A. Liver cancer B. Lung cancer C. Non-Hodgkin lymphoma D. Kidney cancer</p> <p>Answer: D</p> <p>EPA concludes that TCE is characterized as "carcinogenic to humans" by all routes of exposure. This conclusion was based primarily on strong evidence of consistently elevated relative risks between TCE exposure and kidney cancer in humans. The epidemiologic evidence is moderate for non-Hodgkin lymphoma (relative risk estimates were more variable compared with kidney cancer). The epidemiologic evidence of consistency for liver cancer was limited (fewer studies overall, more variable results). There was suggestive evidence for pulmonary tumors from animal studies in mice.</p>

	To review relevant content, see “ <i>Carcinogenic Effects</i> ” in this section (2.2).
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CHAPTER 3. DIAGNOSIS, TREATMENT, AND PREVENTION

Contents	<p>Chapter 3 covers the following topics:</p> <ul style="list-style-type: none"> Section 3.1. Evaluation and diagnosis Section 3.2. Treatment Section 3.3. Regulations and guidelines Section 3.4. Counseling and prevention
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Section 3.1. Evaluation and diagnosis

Learning objective 4	<p>After completing this section, you will be able to</p> <ul style="list-style-type: none"> • Describe possible clinical symptoms and signs in patients exposed to TCE.
Overview	<p>When considering the human health effects of TCE, it is important to make a distinction between occupational exposures to relatively high levels by inhalation and general environmental exposures to low levels in drinking water and ambient air.</p> <p>Symptoms and signs potentially associated with TCE exposure are nonspecific, making a careful medical and exposure history essential to diagnosis.</p> <p>The initial history and physical examination of patients potentially exposed to TCE can be used to</p> <ul style="list-style-type: none"> • determine possible sources and pathways of exposure to TCE, • detect symptoms and signs attributable to TCE exposure, and • reveal history of any preexisting or underlying condition(s) that might complicate the diagnostic and clinical approach to the patient.
Patient history	<p>An exposure history should be part of the patient history. (ATSDR has developed CSEMs on “Taking an Exposure History” and “Taking a Pediatric Exposure History.” To view these CSEMs, and others, go to http://www.atsdr.cdc.gov/csem/.) Taking an exposure history might enable physicians to</p> <ul style="list-style-type: none"> • 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 TCE 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 TCE 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

An occupational history should be routinely obtained. It should include items such as

- company name and location
- job title
- employment dates
- description of chemical processes encountered
- known toxic agents used
- personal protective equipment (PPE) used
- workplace investigations
- complaints of co-workers
- medical monitoring

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.

	<p>Also consider the association between solvent exposure and health conditions (Rom, 2007), such as</p> <ul style="list-style-type: none">• glomerulonephritis,• contact dermatitis,• cognitive impairment, and• peripheral neuropathy. <p>Identify the patient's complaints in terms of</p> <ul style="list-style-type: none">• onset,• duration,• frequency, and• intensity. <p>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.</p>
Physical examination	<p>When performing a physical exam, you might see subclinical, delayed, or individual variability in the initial presentation.</p> <p>Record vital signs, noting any abnormalities of heart rate or rhythm. Examine the head, eyes, ears, nose, and throat, noting any inflammation or irritation.</p> <p>Inspect the skin for signs of dermatitis and defatting changes, especially in the hands. Exam findings might include</p> <ul style="list-style-type: none">• redness,• drying,• cracking, or• fissuring. <p>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.</p> <p>Conduct a mental status examination to evaluate</p> <ul style="list-style-type: none">• alertness,• orientation,• cognition, and• short-term memory.

	<p>Assess nervous system function by evaluating</p> <ul style="list-style-type: none"> • proprioception, • deep tendon reflexes, • cranial nerves, • cerebellar function (nystagmus, finger-nose test, rapid alternating movements, heel-shin test), • motor strength, • gait, • postural stability (Romberg test), and • sensitivity to vibration, light touch, and pin prick.
<p>Signs and symptoms: acute exposure</p>	<p>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. Central nervous system (CNS) symptoms can be similar to those of ethanol inebriation.</p> <p>With inhalation of high concentrations, TCE causes initial CNS excitation, followed by CNS depression. Depending on the duration and intensity of exposure, signs and symptoms can include</p> <ul style="list-style-type: none"> • ataxia, • bronchial irritation, • confusion, • dizziness, • drowsiness, • dyspnea, • euphoria, • fatal cardiac dysrhythmias, • fatigue, • headache, • lethargy, • light-headedness, • pulmonary edema, • renal and hepatic damage, • respiratory depression, • seizures, • stupor, and • visual disturbances. <p>Coma and respiratory depression might occur after prolonged, high-level inhalation exposure (i.e., >2,000 ppm). Serious ventricular arrhythmias can develop up to 24 hours after large TCE ingestions (ATSDR, 2019).</p>

Effects from ingestion of moderate to large amounts of TCE include

- abdominal pain,
- circulatory collapse,
- diarrhea,
- dizziness,
- dysphagia,
- dysrhythmias,
- hallucinations or distorted perceptions,
- headache,
- incoordination,
- jaundice,
- nausea,
- paresthesia,
- partial paralysis,
- somnolence, and
- vomiting.

TCE is a skin irritant and can cause defatting dermatitis of the skin. Systemic sclerosis (scleroderma) has been linked with TCE exposure. Dermal absorption is not likely to be significant if dermatitis is prevented. Vasodilation (“degreasers flush”) and malaise (Stewart & Hake, 1974) recur in workers who drink ethanol after repeated exposure to TCE.

The clinician should keep in mind that, for patients with acute high-dose exposure,

- Respiratory depression and mental status changes are serious effects of acute high-dose TCE exposure. The adequacy of ventilation should be carefully assessed, especially among patients with decreased levels of consciousness. End-tidal capnography and pulse oximetry monitoring might be helpful, if available.
- Because of possible arrhythmias and other cardiovascular effects, consider performing a 12-lead electrocardiogram, frequent evaluation of vital signs, and continuous cardiac monitoring. This might be especially important among patients with preexisting cardiovascular disease.
- Because hepatic injury can occur, liver function tests should be performed.

<p>Signs and symptoms: chronic exposure</p>	<p>The symptoms seen in humans in cases of long-term exposure were similar to those seen in acute exposure, but occurred in more extreme and persistent forms (Fan, 1988; Kleinfeld, 1954). The World Health Organization noted that chronic effects such as disturbance of the nervous system can occur after prolonged exposure to TCE concentrations of about 100 ppm (the current OSHA 8-hour permissible exposure limit [PEL]) (WHO, 1985).</p> <p>Reported neurological effects associated with chronic workplace exposure to TCE have included nonspecific symptoms such as</p> <ul style="list-style-type: none"> • ataxia, • decreased appetite, • dizziness, • emotional instability, • fatigue, • headache, • impaired judgment, • memory loss, • sleep disturbances, and • weakness. <p>Although some CNS symptoms disappear within several weeks after cessation of chronic occupational exposure, other CNS adverse health effects, such as memory loss and mood swings, can persist in persons who have been exposed to TCE for long periods (ATSDR, 2019).</p> <p>Persistent neurological symptoms suggest the possibility of psychiatric disorders and should also prompt a search for exposure to neurotoxicants, such as alcohol and other drugs of abuse.</p>
<p>Laboratory tests: introduction</p>	<p>TCE may be measured to confirm TCE exposure. Keep in mind that although a TCE test might show recent exposure, correlating a TCE level to specific health effects is not possible. Significant exposure to TCE can result in elevated values of routine laboratory tests, including renal and liver function tests, although they are not specific to TCE exposure.</p>
<p>Direct biologic indicators</p>	<p>TCE: Directly testing for TCE in the blood can be used for either immediate exposure or chronic exposure. However, multiple factors can influence these results, including time when the sample was taken, total body fat, activity level, and enzyme activity of aldehyde and alcohol dehydrogenase (Waksman & Phillips, 2004). Detectable plasma levels of TCE in persons without occupational exposure are approximately 0.01 micrograms per deciliter ($\mu\text{g}/\text{dL}$) to 0.13 $\mu\text{g}/\text{dL}$.</p>

	<p>TCE can be detected in the breath and urine up to 16 hours after exposure. It is worth noting that although breath testing conducted soon after exposure can confirm exposure, it is not widely available, so the usefulness is probably limited.</p> <p>TCE metabolites: Although TCE disappears rapidly from the blood, metabolites (e.g., TCA) can persist in the blood for several weeks and in urine up to 3 weeks after heavy exposure (Monster et al., 1979; Sato et al., 1977). Immediate exposure is best measured by trichloroethanol levels in the blood. Chronic exposure is best measured by urinary TCA (Waksman & Phillips, 2004).</p> <p>Caution. The presence of TCE metabolites should be interpreted with caution because some medications (chloral hydrate and disulfiram) and other chlorinated hydrocarbons (1,1,1-trichloroethane and tetrachloroethylene) are also metabolized to TCA and excreted in the urine (ATSDR, 2019).</p> <p>The TCE metabolite, free trichloroethanol, can be measured in the blood. However, several other compounds affect the level of trichloroethanol found in the blood, thereby clouding the clinical significance of this metabolite as an indicator of TCE exposure. Thus, if higher-than-expected blood levels of trichloroethanol are detected, the clinician must consider alternate explanations for the elevated levels.</p>
<p>Indirect biologic indicators: Baseline</p>	<p>Conduct the following testing immediately to establish baseline values if acute exposure to TCE has resulted in marked CNS symptoms such as syncope:</p> <ul style="list-style-type: none"> • Liver function • Blood urea nitrogen (BUN) • Serum creatinine • Urinalysis <p>Repeat testing if any of the results are abnormal, if the patient becomes symptomatic, or if there is any concern for ongoing exposure.</p> <p>Liver function tests should include</p> <ul style="list-style-type: none"> • alkaline phosphatase • alanine aminotransferase (ALT) (serum glutamic-pyruvic transaminase SGPT) <ul style="list-style-type: none"> • aspartate aminotransferase (AST) (serum glutamic-oxaloacetic transaminase SGOT) • bilirubin • lactate dehydrogenase

	<p>Transient elevations of serum levels of liver enzymes have been reported in TCE exposure, but hepatic necrosis is rare. If enzyme levels remain elevated, consider other causes of hepatic dysfunction and initiate appropriate clinical evaluation. Always consider alcohol consumption, infectious causes, nonalcoholic fatty liver disease, and other hepatotoxic xenobiotics in the differential diagnosis when interpreting abnormal liver function test results.</p> <p>Neuropsychological testing might be useful for comparing exposed occupational populations to non-exposed control groups.</p> <p>Contacting an expert in environmental and occupational medicine might provide information, assistance, and referral for clinical evaluation if the exposure history verifies environmental exposures.</p>
<p>Other indirect biologic indicators</p>	<p>Kidneys: Urinary excretion of glutathione-S-transferase alpha (Bruning et al., 1999), α_1-microglobulin (Bolt, Lammert, Selinski, & Bruning, 2004), β_2-microglobulin (Nagaya, Ishikawa, & Hata, 1989), and N-acetyl-β-D-glucosaminidase (Brogren, Christensen, & Rasmussen, 1986; Selden, Hultberg, Ulander, & Ahlberg, 1993) are used to indicate kidney damage, but none of these markers is specific to TCE-induced damage. A number of short-chain halogenated hydrocarbons can produce similar effects [ATSDR 2014]. Research studies have used these indicators to study kidney damage, but some of these are not readily available to clinicians, and the results are not specific to TCE-induced damage.</p> <p>Heart: Electrocardiogram and continuous cardiac monitoring should be considered for heavily exposed persons.</p> <p>Gastrointestinal: Ingestion of large amounts of TCE, which can cause nausea, vomiting, and diarrhea, can produce an electrolyte imbalance.</p> <p>Nervous system: Because the trigeminal, optic, and facial nerves can be impaired by exposure to dichloroacetylene, changes in the visual fields and trigeminal nerve potentials can be noted (Szlatenyi & Wang, 1996).</p> <p>Immune system: If autoimmune disease is suspected, consider expert consultation with a rheumatologist for appropriate serologic testing and other diagnostic workup.</p>
<p>Key points</p>	<ul style="list-style-type: none"> • TCE exposure produces no unique clinical clues. • Respiratory depression can result from acute, high-dose TCE exposure. • At permissible workplace levels, CNS symptoms of TCE exposure, if any, are usually nonspecific and transient. • TCE can be detected in blood, breath, and urine to confirm TCE exposure.

	<ul style="list-style-type: none"> • Urinary proteins, liver function tests, a serum creatinine test, and continuous cardiac monitoring should be considered for persons acutely exposed to high levels of TCE.
Section 3.1: Question #1	<p>A temporal association between signs and symptoms and exposure to TCE is important in the patient exposure history because</p> <ul style="list-style-type: none"> A. It helps evaluate general health B. It helps determine patient history on alcohol and drug use C. It helps provide important clues on the cause D. All of the above <p>Answer: C</p> <p>A temporal relationship between onset of symptoms and work or other activity might provide important clues to the cause. If a temporal association between symptoms and exposure to certain products is suspected, an attempt should be made to identify the specific chemical ingredients involved.</p> <p>To review relevant content, see “<i>Patient history</i>” in this section (3.1).</p>
Section 3.1: Question #2	<p>Symptoms associated with inhalation of high-level TCE include all of the following except</p> <ul style="list-style-type: none"> A. Dyspnea B. Euphoria C. Stupor D. Diarrhea <p>Answer: D</p> <p>Diarrhea is one of the effects from ingestion of TCE.</p> <p>To review relevant content, see “<i>Signs and Symptoms - Acute Exposure</i>” in this section (3.1).</p>
Section 3.1: Question #3	<p>To confirm TCE exposure, which of the following measurements is most reliable?</p> <ul style="list-style-type: none"> A. Trichloroacetic acid in blood and urine B. TCE in breath, blood, or urine C. Elevated values of renal and liver function tests D. Elevated values of routine laboratory tests <p>Answer: B</p>

	<p>If the cause of symptoms is questionable, direct biologic testing, such as measuring TCE level in breath, blood, or urine, might be warranted to confirm TCE exposure.</p> <p>To review relevant content, see “<i>Direct biologic indicators</i>” in this section (3.1).</p>
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Section 3.2. Treatment

Learning objective 4 (cont.)	<p>After completing this section, you will be able to</p> <ul style="list-style-type: none"> • describe treatment following TCE exposure.
Overview	<p>There is no antidote for TCE poisoning. Treatment consists of removing the patient from the exposure and supporting respiratory and cardiovascular functions.</p>
Acute exposure	<p>TCE 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.</p> <p>Additional recommendations include</p> <ul style="list-style-type: none"> • 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 • maintaining good ventilation.
Chronic exposure	<p>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 is found.</p> <p>The level of exposure either must be reduced or the source eliminated for persons with TCE toxicity. Depending on the setting, this might be accomplished by</p> <ul style="list-style-type: none"> • using an agent less hazardous than TCE or • increasing air ventilation.
Key points	<ul style="list-style-type: none"> • TCE poisoning has no antidote; supportive measures should be

	<p>administered.</p> <ul style="list-style-type: none"> • In all suspected cases, removal from exposure should reduce or eliminate symptoms.
Section 3.2: Question #1	<p>All of following statements are correct EXCEPT</p> <p>A. Symptoms related to chronic exposure tend to worsen during exposure and improve when exposure stops.</p> <p>B. The patient should avoid use of alcohol or other CNS depressant medication.</p> <p>C. Supportive care directed to adequate ventilation and circulation should be provided.</p> <p>D. There is a specific antidote for TCE poisoning.</p>
	<p>Answer: D</p> <p>There is no antidote for TCE poisoning. Treatment should focus on removal from exposure and support of respiratory and cardiovascular functions.</p> <p>To review relevant content, see “<i>Chronic Exposure</i>” in this section (3.2).</p>

Section 3.3. Regulations and guidelines

Learning objective 5	<p>After completing this section, you will be able to</p> <ul style="list-style-type: none"> • identify existing regulations and guidelines for TCE in the environment and in the workplace.
Overview	<p>The federal government has developed regulations and guidelines for TCE to protect the public and workers from potential adverse health effects from exposure.</p>
Federal regulations: Environment	<p>Levels of environmental exposure to TCE are generally low and are decreasing because 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 it is not likely to bioaccumulate in the food chain.</p> <p>Air: EPA has identified TCE as one of 33 hazardous air pollutants that present the greatest threat to public health in urban areas (NTP, 2016).</p> <p>Water: The World Health Organization recommended drinking water limit is 30 µg TCE/liter (L) of water (30 ppb) (WHO, 2005). EPA has set a maximum contaminant level (MCL) of 5 µg/L (5 ppb) in drinking water (EPA, 2020).</p>

	<p>Food: The U.S. Food and Drug Administration (FDA) has set maximum permissible level of 5 µg/L of TCE in bottled water. TCE may be used as a solvent in the manufacture of specified foods, with maximum residue levels ranging from 10 ppm to 30 ppm (NTP, 2016).</p>												
<p>Federal regulations: Industry/Workplace</p>	<p>The EPA Toxic Substances Control Act stipulates that manufacturers (including importers) or processors of TCE for use in a consumer product (except for use in cleaners and solvent degreasers, film cleaners, hoof polishes, lubricants, mirror edge sealants, and pepper spray) are required to notify EPA at least 90 days before commencing. That allows EPA to evaluate the intended use and to regulate prospective manufacturers or processors of TCE before the use occurs, provided that regulation is warranted under the act (NTP, 2016).</p> <p>The OSHA permissible exposure limit (PEL) is an 8-hour time-weighted average (TWA) of 100 ppm, with 200 ppm, 300 ppm(peak) TCE for a single time period up to 5 min in any 2 hours. (OSHA, 1993, 2020).</p> <p>The National Institute for Occupational Safety and Health (NIOSH) has a recommended exposure limit (REL) of 25 ppm as a 10-hour TWA for workers. The immediate dangerous to life and health limit is 1,000 ppm (NIOSH, 2020).</p> <p>The American Conference of Governmental Industrial Hygienists recommends 10 ppm as a threshold limit value–time-weighted average (TLV-TWA) and 25 ppm as a TLV–short-term exposure limit (TLV-STEL) (NTP, 2016).</p>												
<p>Summary of current federal regulations and guidelines</p>	<p>Table 1. Federal Regulations and Guidelines for Trichloroethylene</p> <table border="1" data-bbox="483 1444 1421 1900"> <thead> <tr> <th>Agency</th> <th>Focus</th> <th>Level</th> <th>Comments</th> </tr> </thead> <tbody> <tr> <td>American Conference of Governmental Industrial Hygienists</td> <td>Air: workplace</td> <td>10 ppm* 25 ppm</td> <td>Advisory; TLV-TWA[†] Advisory; TLV-STEL[‡]</td> </tr> <tr> <td>National Institute for Occupational Safety and Health</td> <td>Air: workplace</td> <td>25 ppm</td> <td>Recommendation; 10-hour TWA§; potential carcinogen</td> </tr> </tbody> </table>	Agency	Focus	Level	Comments	American Conference of Governmental Industrial Hygienists	Air: workplace	10 ppm* 25 ppm	Advisory; TLV-TWA [†] Advisory; TLV-STEL [‡]	National Institute for Occupational Safety and Health	Air: workplace	25 ppm	Recommendation; 10-hour TWA§; potential carcinogen
Agency	Focus	Level	Comments										
American Conference of Governmental Industrial Hygienists	Air: workplace	10 ppm* 25 ppm	Advisory; TLV-TWA [†] Advisory; TLV-STEL [‡]										
National Institute for Occupational Safety and Health	Air: workplace	25 ppm	Recommendation; 10-hour TWA§; potential carcinogen										

	Occupational Safety and Health Administration	Air: workplace	100 ppm 200 ppm, 300 ppm(peak)	Regulation; PEL [¶] over 8-hour workday Regulation; for a single time period up to 5 min in any 2 hours.
	Environmental Protection Agency	Air: environment	Not available	Not available
		Drinking water	5 ppb**	Regulation
	Food and Drug Administration	Food: bottled water	5 µg /L	Regulation, maximum permissible level
	<p>* ppm = parts per million. [†] TLV-TWA = threshold limit value–time-weighted average; a time-weighted average concentration for a normal 8-hour workday or 40-hour work week to which nearly all workers might be repeatedly exposed. [‡] TLV-STEL = threshold limit value–short-term exposure limit); a 15-minute TWA exposure that should not be exceeded at any time during a workday. [§] TWA = time-weighted average; a concentration for a normal 8-hour workday and 40-hour work week set at a level at which nearly all workers may be repeatedly exposed without adverse effects. [¶] PEL = permissible exposure limit; the highest level averaged over an 8-hour workday to which a worker may be exposed. Note: A PEL of 50 ppm was enacted by Occupational Safety and Health Administration in 1989, but that level, along with 375 others, was vacated for procedural reasons by the 11th Circuit Federal Court in 1993. ** ppb = parts per billion.</p>			
Key points	<ul style="list-style-type: none"> • Environmental exposures to TCE are generally low and are decreasing because limitations have been imposed on its use as an anesthetic, solvent extractant, fumigant, and dry-cleaning agent. • EPA and several other federal agencies have strict regulations on exposure limits of TCE in the environment and in the workplace. 			
Section 3.3: Question #1	<p>All of the following statements regarding U.S. regulations and guidelines for TCE are true except</p> <p>A. Environmental exposures to TCE are generally low and are decreasing so that TCE is not listed as a hazardous air pollutant.</p>			

	<p>B. EPA and FDA have set a maximum limit (5 ppb or 5 µg/L) for TCE in drinking water.</p> <p>C. EPA regulates prospective manufacturers or processors of TCE before the use occurs, if that regulation is warranted under the Toxic Substances Control Act.</p> <p>D. Federal agencies have set strict regulations on exposure limits of TCE in the workplace.</p>
	<p>Answer: A</p> <p>All of the statements are true except A. It is true that environmental exposures to TCE are generally low and are decreasing because limitations have been imposed on its use as an anesthetic, solvent extractant, fumigant, and dry-cleaning agent. However, EPA has identified TCE as one of 33 hazardous air pollutants that present the greatest threat to public health in urban areas.</p> <p>To review relevant content, see this entire section (3.3).</p>

Section 3.4. Counseling and prevention

Learning objective 6	<p>After completing this section, you will be able to</p> <ul style="list-style-type: none"> • describe how to prevent exposure to elevated levels of TCE.
Overview	<p>All patients exposed to TCE need basic guidance on</p> <ul style="list-style-type: none"> • 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	<p>Advise patients to avoid exposures and conditions that might further increase their risk for disease or worsen their existing condition(s).</p> <p>High levels of exposure can occur during cleanup of contaminated equipment and spills and might require use of an approved full-facepiece, self-contained breathing apparatus or other personal protective equipment. Industries and businesses should establish procedures for spill cleanup in advance, including capping all containers of liquid TCE and storing rags soaked with TCE in sealed containers.</p>

	<p>In occupational exposures, the law requires employers or manufacturers to provide pertinent safety data sheets (SDS). The SDS for chemical products list their ingredients, describes their potential toxicity, and suggests precautions for safe use.</p> <p>Advice on self-care for the patient might include the following:</p> <p>At home</p> <ul style="list-style-type: none"> • Use safer alternatives to products with TCE. • When using products containing TCE, ensure plenty of airflow/ventilation (e.g., opening all windows and using fans). • Use appropriate PPE that protects against TCE (e.g., wear a proper respirator or protective gloves, or both) when using products that contain TCE. <p>At work</p> <ul style="list-style-type: none"> • OSHA’s Hazard Communication Standard [OSHA 2012] requires employers to provide labeling, SDS, and safety training on use of chemicals in the workplace. • 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. • Be sure to use the employer-supplied PPE: gloves, goggles, mask, and respirator, as recommended.
<p>Clinical follow up</p>	<p>TCE has been shown to be strongly associated with kidney cancer and to have a moderate association with non-Hodgkin lymphoma. Periodic clinical evaluation might help detect abnormalities at an early stage, if they occur. This would also be true for other TCE-related health effects. Consultation with a specialist in occupational and environmental medicine or others with expertise and experience treating patients exposed to TCE might help you develop a periodic monitoring plan, as appropriate.</p> <p>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.</p> <p>Advise patients to consult you or another physician if they develop signs or symptoms of</p> <ul style="list-style-type: none"> • CNS disorders or • other health changes (especially those possibly related to liver and kidney problems).

<p>Additional information and resources</p>	<p>Refer to the following online resources for more information on the adverse effects of TCE, the treatment of TCE poisoning, and management of persons exposed to TCE. You may also contact ATSDR (see URLs provided below), your state and local health departments, and university medical centers.</p> <p>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.</p> <p>CDC-INFO: 1-800-CDC-INFO (1-800-232-4636); TTY 888-232-6348 24 hours/day email: cdcinfo@cdc.gov.</p> <p>ATSDR Toxicological Profile for Trichloroethylene https://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=173&tid=30</p> <p>ToxFAQs™ for Trichloroethylene https://www.atsdr.cdc.gov/toxfaqs/TF.asp?id=172&tid=30</p> <p>Other Sources of Information</p> <p>American Association of Poison Control Centers Poison Control Hotline: 1-800-222-1222</p> <p>Association of Occupational and Environmental Clinics http://www.aoec.org</p> <p>Pediatric Environmental Health Specialty Units -PEHSUs https://pehsu.net</p> <p>American College of Occupational and Environmental Medicine http://www.acoem.org</p> <p>American College of Medical Toxicologists http://www.acmt.net</p> <p>American College of Preventive Medicine http://www.acpm.org</p> <p>ATSDR Information Center https://www.atsdr.cdc.gov/contacts.html</p> <p>The National Institute for Occupational Safety and Health (NIOSH) https://www.cdc.gov/niosh/topics/trichloroethylene/default.html</p> <p>Other CSEMs</p>
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	<p>“Case Studies in Environmental Medicine: Trichloroethylene 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, go to http://www.atsdr.cdc.gov/csem/csem.html.</p>
<p>Key points</p>	<ul style="list-style-type: none"> • Physicians should advise patients to avoid TCE 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.
<p>Section 3.4 Question #1</p>	<p>Patients who potentially have been exposed to TCE should</p> <ol style="list-style-type: none"> 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 <p>Answer: D</p> <p>If exposures are occupational, patients should speak to their employer about ways to reduce occupational exposure risk. Advise patients to avoid exposures and conditions that might further increase their risk for disease or worsen any existing health conditions. In addition, patients should contact their physician if they develop neurological problems or other health changes.</p> <p>To review relevant content, see “<i>Self-care</i>” and “<i>Clinical follow up</i>” in this section (3.4).</p>

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