

ATSDR Case Studies in Environmental Medicine Polychlorinated Biphenyls (PCBs) Toxicity



**U.S. Department of
Health and Human Services**
Agency for Toxic Substances
and Disease Registry

CASE STUDIES IN ENVIRONMENTAL MEDICINE

Polychlorinated Biphenyls (PCBs) Toxicity

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Key Concepts

- The highest human exposures to polychlorinated biphenyls (PCBs) occur via the consumption of contaminated fish and, in certain occupational settings, via contact with equipment or materials made before 1977.
- Recent studies indicate that maternal consumption of PCB-contaminated fish can cause disturbances in reproductive parameters and neurobehavioral and developmental deficits in newborns and older children.
- Evidence shows that exposures to high concentrations of PCBs cause adverse dermal effects in humans. On the basis of sufficient evidence of carcinogenicity in humans and experimental animals, the International Agency for Research on Cancer (IARC) classified PCBs as carcinogenic to humans (Group 1).

About This and Other Case Studies in Environmental Medicine

This educational case study document is one in a series of self-instructional modules designed to increase the primary care provider's knowledge of hazardous substances in the environment and to promote the adoption of medical practices that aid in the evaluation and care of potentially exposed patients. The complete series of Case Studies in Environmental Medicine is located on the ATSDR Web site at URL: <http://www.atsdr.cdc.gov/csem/csem.html> In addition, the [downloadable PDF](#) version 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.

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U.S. Department of Health and Human Services
Agency for Toxic Substances and Disease Registry
Division of Toxicology and Human Health Sciences
Environmental Medicine Branch

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How to Use This Course

Introduction	The goal of ATSDR's CSEM is to increase the primary health care provider's knowledge of hazardous substances in the environment and to help evaluate and treat potentially exposed patients. This CSEM focuses on PCB toxicity.
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Availability	<p>Two versions of the PCB toxicity CSEM are available.</p> <ul style="list-style-type: none"> • The HTML version http://atsdr-link.cdc.gov/csem/csem.asp?csem=30&po=0 provides content through the Internet. This version offers interactive exercises and prescriptive feedback to the user. • The downloadable PDF version http://www.atsdr.cdc.gov/csem/pcb/docs/pcb.pdf provides content in an electronic, printable format.
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Instructions	<p>To make the most effective use of this course:</p> <ul style="list-style-type: none"> • Take the Initial Check to assess your current knowledge about PCB toxicity. • Read the title, learning objectives, text, and key points in each section. • Complete the progress check exercises at the end of each section and check your answers. • Complete and submit your assessment and posttest response online if you wish to obtain free continuing education credit. You can print your continuing education certificates immediately upon completion.
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Instructional Format	<p>This course is designed to help you learn efficiently. Topics are clearly labeled so that you can skip or quickly scan sections with which you are already familiar. This labeling will also allow you to use this training material as a handy reference. To help you identify and absorb important content quickly, each section is structured in the following format.</p>
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Section Element	Purpose
Title	Serves as a focus question that you should be able to answer after completing the section
Learning Objectives	Describes specific content addressed in each section and focuses your attention on important points
Text	Provides the information you need to answer the focus questions and achieve the learning objectives
Key Points	Highlights important issues and helps you review

Progress Check Exercises	Enables you to test yourself to determine whether you have mastered the learning objectives
Progress Check Answers	Provides feedback to ensure you understand the content and can locate information in the text

Learning Objectives	Upon completion of the PCBs toxicity CSEM, you will be able to meet the objectives as outlined.
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Content Area	Objectives
Overview	<ul style="list-style-type: none"> Describe key characteristics of PCBs
Exposure Pathways	<ul style="list-style-type: none"> Identify sources of exposure to PCBs Identify routes of exposure to PCBs
Who is at Risk	<ul style="list-style-type: none"> Identify who is at risk for exposure to PCBs
Standards and Regulations	<ul style="list-style-type: none"> Identify EPA's maximum contaminant level (MCL) for PCBs in drinking water Identify FDA's tolerance levels for PCBs in food
Biological Fate	<ul style="list-style-type: none"> Describe characteristics of the metabolism of PCBs in the body
Health Effects	<ul style="list-style-type: none"> Describe adverse health effects associated with exposure to PCBs
Clinical Assessment	<ul style="list-style-type: none"> Describe characteristic findings on clinical assessment of patients exposed to PCBs Describe a rational approach for evaluating a patient with a history of occupational or environmental exposure, or both, to PCBs Describe measurements that can help diagnose exposure to PCBs
Treatment and Management	<ul style="list-style-type: none"> Describe the principal treatment strategy for managing PCB poisoning Describe the measures for preventing occupational and environmental exposure to PCBs

Patient
Education and
Counseling

- Describe instructions appropriate for patients exposed to PCBs
-

Initial Check

Instructions

This Initial Check will help you assess your current knowledge about PCB toxicity. To take the Initial Check, read the case below and then answer the questions that follow.

Case

A 48-year-old handyman has progressive cystic acne and abnormal liver function.

A 48-year-old man that you are treating for acne vulgaris returns to your clinic for a follow-up appointment. You first saw this patient about 3 weeks ago. At that time, he had multiple acneiform lesions in the malar and periorbital areas. Both cystic and comedonal lesions were present; most ranged between 3 and 6 millimeters (mm) in diameter, and some were edematous. The patient noted that he was surprised about the development of acne at his age; he never suffered from this condition during adolescence. He had used over-the-counter astringents and anti-acne medications, but they had not affected the lesions.

A review of the patient's medical history indicates that he has

- **No** history of hepatitis,
- **No** recollection of contact with hepatitis patients,
- **No** evidence of liver difficulties, and
- **No** record of blood transfusion.

The patient has no family history of cardiovascular disease or cancer. The patient does not smoke; he drinks two to three bottles of beer each evening and sometimes more on weekends. He is taking no medications other than over-the-counter dermatologic medications.

The patient is married and has three teenaged children.

His wife and children are in good health. They live in a high-rise apartment building where the patient has been a handyman and part-time building manager for the past year. He spends a lot of time in the basement area, which includes

- Heating facilities,
- A laundry,
- A recreation room with pool table, and
- A workshop.

The patient is an avid fisherman who spends most weekends fishing and eating his catch with his two sons.

At the end of the patient's initial visit, you prescribed a topical antibiotic and instructed the patient on its use. After reassuring the patient that stronger prescription medications are available to treat acne, you ordered a serum biochemical and hematologic profile to document baseline values.

During today's physical examination, you note little or no improvement in the patient's acne. The ratio of cystic to comedonal lesions appears to have increased, and many lesions appear to have become more edematous and erythematous. The patient has several new comedones on his chin, and he points out what appears to be developing areas of folliculitis on his chest and forearms.

In addition to this worsening of the patient's acne, your physical examination of the patient reveals mild, non-tender hepatomegaly without jaundice. This finding causes you to review the results of the biochemical panel. You note the following abnormalities:

- Total bilirubin 2.8 milligrams per deciliter (mg/dL) (normal 0–1.5),
 - Direct bilirubin 0.4 mg/dL (normal 0–0.4),
 - Serum glutamic-pyruvic transaminase (SGPT) (alanine aminotransferase [ALT]) 74 international units per liter (IU/L) (normal 0–50),
 - Serum glutamic-oxaloacetic transaminase (SGOT) (aspartate aminotransferase [AST]) 88 IU/L (normal 0–50),
-

-
- Glutamyl transpeptidase (GGTP or GGT) 190 IU/L (normal 15–85), and
 - Lactate dehydrogenase (LDH) 230 IU/L (normal 50–225).

The results of all other tests, including the complete blood count, alkaline phosphatase (ALP), blood urea nitrogen, creatinine, and urinalysis, are within normal limits.

Initial Check Questions

1. What should be included in the patient's problem list?
2. What is a differential diagnosis for the patient's altered liver enzymes?
3. What tests would help you arrive at a diagnosis?
4. You persistently pose detailed questions to the patient regarding his work, hobbies, recreational activities, and possible contact with hepatotoxins.

The patient reveals that he frequently wipes up a "dark, oily discharge" near a large electrical transformer in the work area in the basement workshop. The discharge has produced a gummy residue on tools and other surfaces. He mentions he sometimes feels dizzy and nauseated after working in the basement all day.

Is this additional information related to the clinical findings?

5. Is there a need to be concerned about exposure to PCBs when the clinical effects in this patient seem so limited?
 6. Are other sources of PCB exposure likely for this patient?
 7. What confirming laboratory test can be conducted to establish the diagnosis of PCB exposure?
 8. The doctor requests a serum PCB analysis. The laboratory reports a level of 125 parts per billion (ppb), with no normal range indicated. How will you interpret this report?
 9. What steps should be recommended to patients when PCB-related health effects are suspected?
 10. What additional steps should be taken for the situation described in the case study?
-

**Initial Check
Answers**

1. The patient's problem list includes acne vulgaris, which is atypical because of the location of the lesions and their late onset with no history of outbreaks during adolescence. The mildly altered liver functions are nonspecific but clinically unexpected.

More information for this answer can be found in the "Clinical Assessment – Signs and Symptoms" section.

2. The combination of asymptomatic hepatomegaly and mild nonspecific elevations of hepatic enzymes suggests a chronic inflammatory liver process or hepatitis. Hepatitis can be drug-induced, toxic, infectious, genetic, or caused by connective tissue disease.

The major cause of liver disease in the United States is ethanol ingestion. Less commonly, environmental exposures cause either acute or chronic toxic hepatitis. Some connective tissue diseases such as lupus erythematosus are associated with a specific type of hepatitis. Infectious hepatitis includes those attributed to the viruses such as A, B, C, and other possible agents of non-A, non-B hepatitis. Hepatitis can also occur with Epstein-Barr virus and cytomegalovirus infections. Infiltrative diseases such as sarcoidosis or amyloidosis, and rare genetic diseases such as Wilson disease, primary hemochromatosis, and alpha-1-antitrypsin deficiency should be excluded as causes of hepatitis also.

More information for this answer can be found in the "Clinical Assessment – Laboratory Tests" section.

3. Repeat ALT, AST, GGT, and bilirubin testing; test ALP and prothrombin time; and test for hepatitis viral serologies, heterophil antibody (anti-EBV capsid IgM), anti-nuclear antibody, anti-smooth muscle antibody, and anti-mitochondrial antibody. Consider hemochromatosis (serum ferritin, iron, and iron binding capacity), Wilson disease (serum copper and ceruloplasmin), and parasitic hepatitis as possible
-

causes of chronic hepatitis.

Assays for suspected hepatotoxins and biopsy of adipose tissue might also be of value. Further evaluation might include ultrasound and percutaneous liver biopsy if other tests do not provide sufficient information.

More information for this answer can be found in the "Clinical Assessment – Laboratory Tests" section.

4. Older electrical transformers and capacitors can contain PCBs as a dielectric and heat-transfer fluid. Leaks in this equipment could allow PCBs to volatilize under conditions of increased temperature. A person with chronic exposure to the vapors or residue could eventually receive a significant PCB dose through both dermal and inhalation routes.

More information for this answer can be found in the "How Are People Exposed to PCBs?" section.

5. Notably, potential carcinogenicity is the main reason PCB production was banned in the United States. EPA has determined that PCBs are probable human carcinogens and has assigned them the cancer weight-of-evidence classification B2. DHHS concluded that PCBs are reasonably anticipated to be carcinogenic in humans, based on sufficient evidence of carcinogenicity in animals. In February 2013, 26 experts from 12 countries met at the International Agency for Research on Cancer (IARC), Lyon, France, to reassess the carcinogenicity of polychlorinated biphenyls (PCBs). On the basis of sufficient evidence of carcinogenicity in humans and experimental animals, the IARC classified PCBs as carcinogenic to humans (Group 1). The classification is based on consistent association between PCB exposure and increased risk of melanoma in humans.

More information for this answer can be found in the "What Are the Physiologic Effects of PCBs?" section.

-
6. In addition to possible dermal and inhalation exposure, the patient might be exposed by consuming contaminated fish, a potential source of PCBs.

More information for this answer can be found in the "How Are People Exposed to PCBs?" section.

7. Select laboratories have the capability to perform PCB analyses on human tissue. The lipophilic nature of PCBs causes them to accumulate in fat; consequently, analysis of adipose tissue obtained by biopsy has been advocated as a measure of long-term exposure. Serum PCB analysis, which is less invasive than fat biopsy, is readily available. Health risks are not consistent necessarily with PCB levels, but a serum measurement is useful for gauging the patient's exposure.

More information for this answer can be found in the "Clinical Assessment – Laboratory Tests" section.

8. A correlation between increasing levels of serum PCBs and dermatologic findings, including chloracne, has not been found consistently in human epidemiologic studies. However, statistically significant associations between dermatologic effects and plasma levels of higher chlorinated PCB congeners have been reported.

PCB compounds generally can be found at the parts per trillion (ppt) levels in the lipid stores of humans, especially persons living in an industrialized society. The general population is exposed to PCB compounds primarily through the ingestion of high-fat foods such as dairy products, eggs, animal fats, and some fish and wildlife [CDC 2009b; Hopf et al. 2009; Patterson et al. 2008]. By comparison, the case study patient's PCB serum level of 125 ppb is consistent with PCB exposure as a cause for his unusual acne, and PCB exposure might be contributing to the hepatic effects noted.

More information for this answer can be found in the

“Clinical Assessment – Laboratory Tests” section.

9. The first objective should be to stop the exposure. In this case, the patient should stay away from the basement until the transformer is repaired and the basement area is cleaned by a professional familiar with PCB removal. He should also check with his state advisory on PCB-fish contamination and not eat fish from contaminated areas until his PCB level normalizes and the fish are declared uncontaminated. Many states issue advisories on fish consumption based on where the fish are caught. Fish advisories also provide guidance on how to choose fish that are safer to eat and on safer ways to prepare and cook fish. Avoiding exposure is especially important because no specific treatment exists for PCB accumulation. The need to avoid other hepatotoxic substances, including ethanol, should be stressed. Confirmation of exposure with a serum PCB level should be obtained.

More information for this answer can be found in the “How Should Patients Exposed to PCBs Be Treated and Managed?” section.

10. Because stopping exposure is of prime importance, the physician can be most helpful by advising the patient that proper abatement by professionals is necessary. In this case, the owner of the building should be notified of the potential health hazard and should contact the local public health agency. This might require the assistance of local, state, or federal agencies such as the department of public health and EPA. These agencies can cooperate with entities involved to ensure remediation of the harmful exposure. It is important to prevent other persons from using the basement areas until cleanup is complete. In addition, the patient should be informed of the availability of fishing and game advisories particular to his state, and he should be encouraged to observe the recommendations of these advisories.

More information for this answer can be found in the

“How Should Patients Exposed to PCBs Be Treated and Managed?” section.

What Are Polychlorinated Biphenyls (PCBs)?

Learning Objective

Upon completion of this section, you will be able to

- Describe key characteristics of PCBs.

Definition

PCBs are chemicals formed by attaching one or more chlorine atoms (at the Xs in Figure 1 below) to a pair of connected benzene rings.

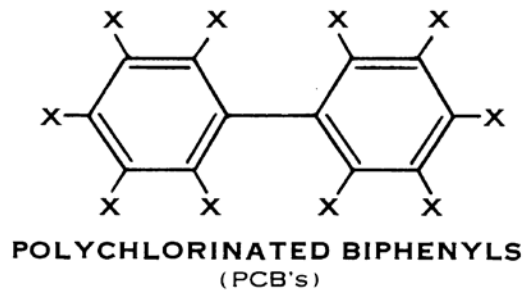


Figure 1: Polychlorinated Biphenyls (PCBs)

Depending on the number and position of chlorine atoms attached to the biphenyl ring structure, 209 different PCB congeners can be formed. PCB congeners can be divided into the coplanar, the mono-ortho-substituted PCBs, and other non-dioxin-like PCBs. The significance of this designation is that coplanar and some of the mono-ortho-substituted PCBs have dioxin-like toxicologic effects.

Chemical Properties: Dioxin-like vs. Non-dioxin-like The chlorination pattern of the PCBs determines the toxicity of the substance. A number of PCB congeners show **dioxin-like** toxicity. These PCBs have no more than one chlorine atom at the ortho-position (polychlorinated non-ortho and mono-ortho biphenyls). The phenyl rings of these molecules can rotate and adopt a coplanar structure, which leads to the same toxicity as the polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs). The toxic effects of these dioxin-like PCBs are discussed in detail in later sections of this document.

A number of PCB congeners, however, have two or more of the ortho-positions in the biphenyl molecules occupied by chlorine molecules. For these, the two phenyl rings are not in the same plane, and these PCBs express **non-dioxin-like** toxicity.

Commercial PCB products are mixtures of different PCB congeners and contain small amounts of PCDFs or PCDDs. Contamination is a concern because the toxicity of these contaminants is generally much greater than that of PCBs [ATSDR 2000].

Uses Because of their insulating and nonflammable properties, PCBs were marketed for nearly 50 years between 1929 and 1977. They were used in making

- Diffusion pump oils,
- Extenders for pesticides,
- Heat exchange and dielectric fluids in transformers and capacitors,
- Hydraulic and lubricating fluids, and
- As ingredients in caulking compounds, paints, adhesives, flame retardants, and plasticizers.

In 1977, the United States banned production of PCBs because of their potential carcinogenicity.

Trade Names The following trade names are used for commercial PCB mixtures:

- Aroclor
-

-
- Asbestol
 - Askarel
 - Clorphen
 - Diaclor
 - Dykanol
 - EEC-18
 - Eucarel
 - Nepolin
 - Pyranol

Key Points

- PCBs are manufactured chemicals produced for nearly 50 years in the United States before they were banned in 1977.
- PCBs were banned because of their potential carcinogenicity.

Progress Check

1. Select the best answer from the following choices:

- A. Commercial PCB products are mixtures of different PCB congeners.
- B. Commercial PCB products commonly are contaminated with small amounts of polychlorinated dibenzofurans (furans) or polychlorinated dibenzodioxins (dioxins).
- C. PCB manufacturing was banned in the United States in 1977.
- D. All of the above.

To review relevant content, see "Chemical Properties and Uses" in this section.

Where Are PCBs Found?

Learning Objective

Upon completion of this section, you will be able to

- Identify sources of exposure to PCBs.
-

Introduction

No known natural sources of PCBs exist. The United States banned production of these chemicals in 1977, when their ability to accumulate in the environment and to cause harmful effects became apparent [ATSDR 2000]. Today, the major source of exposure to ambient PCBs is environmental cycling of PCBs previously released into the environment.

Released Into the Environment

Between 1929 and 1977, more than 1.25 billion pounds of PCBs were produced in the United States [ATSDR 2000]. PCBs can be released into the general environment by or from

- Disposal of PCB-containing consumer products in municipal landfills
- Illegal or improper dumping of waste that contained PCBs, such as transformer fluids
- Leaks (fugitive emissions) from electrical transformers and capacitors containing PCBs
- Poorly maintained toxic waste sites

Once released into the environment, PCBs

- bioaccumulate and biomagnify as they move up the food chain,
- degrade relatively slowly, and
- are cycled and transported within the ecosystem [ATSDR 2000; Safe 2007].

PCBs have been identified in at least 500 of the 1,598 hazardous waste sites on the EPA's National Priorities List, and low levels of PCBs can be found throughout the world [ATSDR 2000].

Environmental Contamination

Once released into the environment, PCBs adsorb strongly to soil and sediment. As a result, these compounds tend to persist in the environment, with half-lives for most congeners ranging from months to years. PCBs leach from soil slowly, particularly the more highly chlorinated congeners, and translocate to plants via soil insignificantly.

Cycling of PCBs through the environment involves volatilization from land and water surfaces into the atmosphere, with subsequent removal from the atmosphere by wet or dry deposition, then revolatilization. In the general population, inhalation of these airborne PCBs is one route of exposure, in addition to the food source of exposure to PCBs.

Key Points

- Environmental contamination from PCBs has been caused by accidental releases, careless disposal practices, and leaks from industrial facilities or chemical waste-water disposal sites.
- PCBs degrade very slowly, are cycled and transported within the ecosystem, and bioaccumulate as they move up the food chain.

Progress Check

2. Once released into the environment, PCBs may undergo all of the following **EXCEPT**
- A. Volatilization from land and water surfaces into the atmosphere
 - B. Biotransformation into more complex undefined mixtures
 - C. Fast degradation within the ecosystem
 - D. Strong adsorption to soil and sediment

To review relevant content, see "Released into Environment" in this section.

What Are Routes of Exposure for PCBs?

Learning Objective

Upon completion of this section, you will be able to

-
- Identify routes of exposure to PCBs.
-

Introduction

Although PCBs are no longer manufactured in the United States, people can still be exposed to them. The two main sources of exposure to PCBs are the environment and the workplace.

Because they are resistant to degradation, highly chlorinated PCB compounds can persist in the environment for decades. However, over the past two decades, concentrations of PCBs in most environmental media generally have decreased.

Non-Occupational Exposure:

- **General Population**

Food is the main source of exposure to PCBs for the general population (CDC 2009b). Exposure occurs primarily by ingesting high-fat foods—such as dairy products, eggs, and animal fats—and some fish and wildlife [ATSDR 2000; CDC 2009b; Fisher 1999; Gunderson and Gunderson 1988; Hopf et al. 2009; Patterson et al. 2008].

CDC publishes the National Report on Human Exposure to Environmental Chemicals. This report is an ongoing assessment of the exposure to environmental chemicals in the general U.S. population. The Fourth Report (CDC 2009b) contains data for years 1999–2000, 2001–2002, and 2003–2004 from participants in National Health and Nutrition Examination Survey (NHANES). Detailed information on NHANES is available at http://www.cdc.gov/nchs/nhanes/about_nhanes.htm.

Serum concentrations of PCBs were found to reflect cumulative past exposure in the general U.S. population [ATSDR 2011].

<ul style="list-style-type: none"> • Bio-accumulation and Dietary Exposure 	<p>In aquatic environments, the high lipophilicity of PCBs causes these compounds to partition out of the water and become adsorbed preferentially to sediments. Although sediment adsorption helps prevent the contamination of drinking-water supplies, the partitioning of PCBs to sediments plays a role in the tendency of these compounds to become concentrated in aquatic organisms. Bottom-feeding fish ingest and accumulate PCBs from sediment. The resistance of these compounds to biodegradation causes PCBs to become more concentrated as they move upward through the food chain from the bottom-feeding organisms. As a result of this bioconcentration and biomagnification, PCB levels in aquatic organisms can be as much as one million times higher than the levels in the aquatic environment [ATSDR 2000].</p> <p>In the National Study of Chemical Residues in Fish conducted between 1986 and 1989 [EPA 1992a, 1992b], the mean concentration of PCBs in bottom-feeding and game fish was 1.9 parts per million (ppm). However, PCB levels as high as 20 ppm have been detected in game fish taken from waters near hazardous waste sites [ATSDR 2000].</p>
<ul style="list-style-type: none"> • FDA Studies 	<p>The U.S. Food and Drug Administration (FDA)'s Total Diet Studies have revealed that total PCB levels have shown a downward trend in concentration from the middle 1970s to the middle 1980s and a relatively steady intake from 1982 to 1997. For example, total diet studies conducted from 1982 to 1984 for adults between the ages of 25 and 30 indicated that the mean daily intake of PCBs was <0.001 micrograms/kilograms ($\mu\text{g}/\text{kg}$) body weight/day while in the 1997 study, the mean was 0.002 $\mu\text{g}/\text{kg}$ body weight/day [ATSDR 2000].</p>
<p>Non-Occupational Exposure:</p> <ul style="list-style-type: none"> • Special populations 	<p>People living near incinerators, other PCB-disposal facilities, or NPL hazardous waste sites where PCBs have been detected may receive higher PCB exposures than the general population. These exposures may be through ingestion, inhalation, or skin contact [ATSDR 2000].</p>

Do-it-yourselfers repairing or removing older construction materials, including plaster, paint, and caulk, that contain PCBs.

Occupational Exposures:

Occupational exposure to PCBs occurs mainly via the inhalation and dermal routes.

- **Inhalation and Dermal**

Commercial PCB mixtures vary from colorless to dark brown oils, and from viscous liquids to sticky resinous semisolids. Although PCBs evaporate slowly at room temperature, the volatility of PCBs increases dramatically with even a small rise in temperature. Equipment that contains PCBs can overheat and vaporize significant quantities of these compounds, creating an inhalation hazard that can be magnified by poor ventilation.

Because of their highly lipophilic nature, PCBs also can be absorbed through the skin following contact with contaminated equipment, water, or soil.

Products that contain PCBs are no longer manufactured, thus occupational exposure no longer occurs in those settings. However, it might occur

- During the maintenance or repair of old equipment that contains PCBs,
- As a result of accidents involving such equipment [Schechter AJ and Charles 1991; Wolff 1985], or
- During waste-site cleanup or disposal activities [ATSDR 2000; Luotamo et al. 1993; Schechter A et al. 1994].
- During repair or removal of older construction materials, including plaster, paint, and caulk that contain PCBs.

Today, PCBs are found mainly in transformers and capacitors manufactured before 1977. Such transformers and capacitors might be found in

- Old industrial equipment (e.g., welding equipment),
 - Medical equipment (e.g., x-ray machines), and
 - Household appliances (e.g., refrigerators,
-

microwaves and televisions).

Key Points

- The primary route of exposure to PCBs in the general population is the consumption of contaminated foods, particularly meat, fish, and poultry.
- Occupational exposure to PCBs occurs mainly via the inhalation and dermal routes.
 - Although occupational exposure no longer occurs as a result of the manufacture of PCB-containing products, it might still occur during the maintenance or repair of equipment manufactured before 1977 that may contain PCBs or as a result of accidents involving such equipment.
 - Occupational exposure might also occur during waste-site cleanup or disposal activities.

Progress Check

3. Which of the following statements is **NOT CORRECT**?

- A. The primary route of exposure to PCBs in the general population is consuming contaminated foods.
- B. Over the past two decades, the general overall trend is decreasing concentrations of PCBs in most environmental media.
- C. Over the past two decades, PCB body burdens in humans have shown no changes.
- D. Occupational exposure to PCBs occurs mainly via the inhalation and dermal routes.

To review relevant content, see "Non-occupational and Occupational Exposure Routes" in this section.

Who Is at Risk of Exposure to PCBs?

Learning Objective

Upon completion of this section, you will be able to

- Identify who is at risk of exposure to PCBs.
-

Introduction

People with potentially high exposures to PCBs include

- Recreational and subsistence fishers who typically consume larger quantities of locally caught fish than the general population,
- Children with in utero and lactational exposure to PCBs from mothers who eat large quantities of contaminated fish during pregnancy and while nursing,
- Certain farmers and their families who consume PCB-contaminated food via their own farm-raised beef and dairy cattle, and
- People living near incinerators, other PCB-disposal facilities, or NPL hazardous waste sites where PCBs have been detected.

Although PCBs are no longer manufactured in the United States, workplace exposure potentially may exist. In occupational settings, persons who repair and maintain equipment with capacitors and transformers manufactured before 1977 could be exposed to PCBs.

**Recreational
and
Subsistence
Fishers**

Due to the factors of culture and lifestyles, sport anglers and subsistence fishers may consume 10 times more fish and seafood than average U.S. consumers. Many of these subsistence fishers are American Indian, ethnic minority, or immigrant populations.

The special dietary practices of these populations can lead to significant exposures to persistent pollutants [Hovinga et al. 1993; Judd et al. 2004].

Children with Maternal Exposures**Children of mothers who eat large quantities of contaminated fish may be exposed to PCBs prenatally and while breastfeeding.**

Several studies have reported that prenatal exposure to PCBs has been confirmed among children of consumers of contaminated fish and certain other groups [Fein et al. 1984; Jacobson JL et al. 1990b; Jacobson SW et al. 1985; Swain and Swain 1991]. Other studies have indicated that lactating women whose diets are high in PCB-contaminated fish potentially can increase the PCB exposure for their breastfeeding infants [Dewailly et al. 1989; Fitzgerald et al. 1998; Greizerstein et al. 1999; Rogan et al. 1985]. Fetuses and neonates are more sensitive to PCBs than are adults. During these early life stages, the hepatic microsomal enzyme systems that facilitate the metabolism and excretion of PCBs are not fully functional.

Farming Families**Farmers and their families who consume PCB-contaminated food via their own farm-raised beef and dairy cattle may be exposed.**

During the 1940s and 1950s, the insides of concrete silos on many farms in the Midwest United States were coated with sealants containing PCBs. Over time, these sealants peeled off and became mixed with silage used to feed beef and dairy cattle. Farmers and their families who lived on these farms and who regularly ate farm-raised beef and dairy products were exposed to PCBs. Although most of these silos have been dismantled and removed, the remaining silos represent a potential source of exposure to PCBs [Hansen 1987; Humphrey 1983; Schantz et al. 1994].

People Living Near PCB Contaminated Sites	Persons living near incinerators, other PCB-disposal facilities, or NPL hazardous waste sites where PCBs have been detected may be exposed.
	Persons living near incinerators, other PCB-disposal facilities, or any of the 500 current or former hazardous waste sites on the NPL sites where PCBs have been found may be also at increased risk for exposure to PCBs [ATSDR 1987; Hazdat 2000; Hermanson and Hites 1989; Robertson and Ludewig 2011; Stehr-Green et al. 1988; Wester et al. 1993].
Persons with Impaired Hepatic Function	PCBs are metabolized mainly in the liver, thus, persons with impaired hepatic function might be at increased risk because their ability to detoxify and excrete these compounds is diminished.
	Persons with incompletely developed glucuronide conjugation mechanisms (such as Gilbert syndrome or Crigler-Najjar syndrome) have impaired liver function, as do persons with chronic liver diseases such as cirrhosis or hepatitis B [Calabrese et al. 1977; Lester et al. 1964].
	Similarly, because hepatic function normally declines with age, elderly persons may be more susceptible to the effects of exposure to PCBs.
Children's Susceptibility	Infants and young children consume a greater amount of food per kilogram of body weight than do adults. Therefore, they have proportionately greater exposure to PCBs than do adults eating food with the same level of contamination [ATSDR 2000]. In addition, as mentioned earlier, fetuses and neonates are potentially more sensitive to PCBs than are adults because their hepatic microsomal enzyme systems that facilitate the metabolism and excretion of PCBs are not fully functional.
Exposure in the Workplace	PCB levels in blood and body tissues were 10–1,000 times higher in persons exposed to PCBs in the workplace than in non-occupationally exposed persons [Kreiss and Kreiss 1985; Wolff 1985; Yakushiji et al. 1978].
	The United States no longer produces PCBs or products

containing PCBs (e.g., capacitors, transformers, and electrical equipment), thus occupational exposure to PCBs no longer occurs in those settings. However, workers can have inhalation or dermal contact with PCBs when repairing or performing routine maintenance on older equipment or electrical transformers, and during accidents or spills involving PCBs [Fait et al. 1989; Schechter AJ and Charles 1991; Welsh 1995; Wolff 1985]. Exposure can also occur during the disposal of materials containing PCBs at hazardous waste sites, waste-site cleanup, or demolishing buildings containing PCBs [Luotamo et al. 1993; Robertson and Ludewig 2011].

Specific occupations with risk for exposure to PCBs in the National Occupational Exposure Survey (NOES)[NIOSH 1989] include

- Construction work,
- Demolition work,
- Electric cable repair,
- Electroplating,
- Emergency response,
- Firefighting,
- Hazardous waste hauling or site operation,
- Heat exchange equipment repair,
- Maintenance or cleaning,
- Medical laboratory technician or technologist,
- Metal finishing,
- Non-cellulose fiber industry,
- Paving and roofing,
- Pipefitting or plumbing,
- Semiconductor and related industries,
- Timber products manufacturing,
- Transformer or capacitor repair, and
- Waste-oil processing.

-
- Farm families who eat PCB-contaminated food; and
 - Persons who live near incinerators, other PCB-disposal facilities, or NPL hazardous waste sites where PCBs have been detected.
 - Persons with compromised hepatic function might metabolize PCBs less efficiently than healthy persons.
 - Although the United States no longer manufactures PCBs, workers can be exposed to PCBs during repair of equipment manufactured before 1977, accidents or spills involving PCB, and waste-site cleanup or disposal activities.

Progress Check 4. Of the following, who may be at increased risk of high-level exposure to PCBs?

- A. Sport anglers and subsistence fishers.
- B. Workers whose jobs include routine maintenance of equipment or electrical transformers manufactured before 1977.
- C. The children of mothers who eat large quantities of contaminated fish during pregnancy and while nursing.
- D. All of the above.

To review relevant content, see all topics in this section.

What Standards and Regulations Exist for PCB Exposure?

Learning Objective

Upon completion of this section, you will be able to

- Describe EPA's maximum contaminant level (MCL) for PCBs in drinking water.
 - Describe FDA's tolerance levels for PCBs in food.
-

Introduction

The U.S. government has developed standards and regulations for PCBs that are designed to protect the public and workers from potential adverse health effects.

Workplace Standards**Air**

The Occupational Safety and Health Administration (OSHA)'s permissible exposure limit (PEL) is a time-weighted average (TWA) airborne concentration of 1.0 milligrams per cubic meter (mg/m^3) for PCBs containing 42% chlorine (average molecular formula of $\text{C}_{12}\text{H}_7\text{Cl}_3$). The PEL for PCBs with 54% chlorine and an average molecular formula of $\text{C}_{12}\text{H}_5\text{Cl}_5$ is $0.5 \text{ mg}/\text{m}^3$ (OSHA 1998a).

Both standards encompass all physical forms of these compounds:

- Aerosols,
- Vapor,
- Mist,
- Sprays, and
- PCB-laden dust particles.

OSHA recognizes that PCBs can be absorbed through intact skin; therefore, both dermal and inhalation exposure routes should be evaluated by an industrial hygienist.

The National Institute for Occupational Safety and Health (NIOSH)FDA recommends a 10-hour TWA of 1.0 micrograms per cubic meter ($\mu\text{g}/\text{m}^3$) based on the minimum reliable detectable concentration and the potential carcinogenicity of PCBs [NIOSH 2005].

NIOSH also recommends that all workplace exposures be reduced to the lowest feasible level.

Environmental Drinking Water Standards

EPA considers PCBs a probable human carcinogen and prohibits industrial discharges under the Clean Water Act Effluent Guidelines.

EPA's goal for drinking water's maximum contaminant level is zero, and the enforceable MCL for PCBs in public water systems is 0.0005ppm [EPA 2001].

EPA requires that PCB spills or accidental releases into the environment of 1 pound or more be reported to EPA [ATSDR 2000].

Food

FDA mandates tolerances of 0.2–3.0 ppm PCBs for all foods, with a tolerance level in fish of 2 ppm. FDA also limits PCBs in paper food-packaging materials to 10 ppm [FDA 1996c].

The Food and Agriculture Organization (FAO) and the World Health Organization (WHO) allow a daily PCB intake of 6 µg/kg per day [AAP 2003].

Table 1. Standards, regulations, and recommendations for PCBs

Agency	Focus	Level	Comments
OSHA	Air: workplace	1.0 mg/m ³ for PCBs with 42% Cl 0.5 mg/m ³ for PCBs with 54% Cl	Enforceable; TWA*, PEL† Both standards encompass all physical forms of aerosols, vapor, mist, sprays, and PCB-laden dust particles.
NIOSH	Air: workplace	1.0 µg/m ³	Advisory; TWA (10-hour)

EPA	Drinking water: environment	0.0005 ppm	Enforceable MCL‡
FDA	Food: environment	0.2–3.0 ppm (all foods) 2.0 ppm (fish) 10 ppm (paper food- packaging materials)	Enforceable; Tolerance level
WHO FAO	Food: environment	6.0 µg/kg per day	Allowable daily intake
<p>*TWA (time-weighted average): TWA concentration for a normal workday and a 40-hour workweek to which nearly all workers may be repeatedly exposed</p> <p>†PEL (permissible exposure limit): highest level of PCBs in air to which a worker may be exposed, averaged over an 8-hour workday</p> <p>‡MCL (maximum contaminant level): enforceable level for drinking water</p> <p>µg/kg: microgram per kilogram</p> <p>µg/m³: microgram per cubic meter</p> <p>ppm: parts per million</p>			

Key Points

- OSHA's PEL is 1,000 µg/m³ for PCB mixtures 42% chlorinated and 500 µg/m³ for compounds 54% chlorinated.
- EPA's enforceable MCL for PCBs in public drinking-water systems is 0.0005 ppm.
- FDA's tolerance levels for PCBs in food range between 0.2 and 3 ppm.

**Progress
Check**

5. Which of the following statements is **FALSE** regarding U.S. standards for PCBs levels?
- A. EPA has set an enforceable MCL for PCBs in public drinking water systems.
 - B. EPA considers PCBs a probable human carcinogen and prohibits industrial discharges under the Clean Water Act Effluent Guidelines.
 - C. FDA has banned PCBs in paper food-packaging materials.
 - D. NIOSH recommends that all workplace exposures to PCBs be reduced to the lowest feasible level.

To review relevant content, see "Environmental Standards" in this section.

What Is the Biologic Fate of PCBs in Humans?

**Learning
Objective**

Upon completion of this section, you will be able to

- Describe the characteristics of PCB metabolism in humans.

Introduction

Rates of PCB metabolism vary greatly with the degree of chlorination of the biphenyl rings and the positions of the chlorines on these rings.

In the environment, PCBs undergo environmental alterations through

- Partitioning,
- Chemical transformation, and
- Preferential bioaccumulation.

As a result, compositions of environmental PCB mixtures differ from commercial PCB mixtures (original Aroclors).

Absorption and Distribution

Humans can absorb PCBs by the:

- Inhalation,
- Oral, and
- Dermal routes of exposure.

Although PCBs are readily absorbed into the body, they are slowly metabolized and excreted.

PCBs initially distribute preferentially to the liver and muscle tissue.

PCBs, especially the highly chlorinated congeners, tend to accumulate in lipid-rich tissues due to their lipophilic nature. Greater relative amounts of PCBs are usually found in

- Adipose tissue,
- Breast milk,
- The liver, and
- Skin [ATSDR 2000; Matthews et al. 1984].

Metabolic Pathways

The liver is the primary site of metabolism of PCBs, which occurs via hydroxylation and conjugation with glucuronic acid and sulfates.

PCBs are metabolized by the microsomal monooxygenase system catalyzed by cytochrome P-450 to phenols (via arene oxide intermediates), which can be conjugated or further hydroxylated to form a catechol [Safe SH 2007]. Glucuronide and sulfate conjugates are excreted mainly in the urine, whereas hydroxylated metabolites are excreted mainly in the bile.

The rate of individual congener metabolism depends on the number and position of chlorine atoms. Steele et al. estimated the half-life in humans for lower chlorinated biphenyls (Aroclor 1242) as 6–7 months and the corresponding half-life for the more highly chlorinated biphenyls as 33–34 months [Steele et al. 1986]. Phillips et al. measured total PCBs in capacitor workers and calculated half lives of 2.6 and 4.6 years for the lower (Aroclor 1242) and higher (Aroclor 1254) chlorinated

biphenyls, respectively [Phillips et al. 1989]. A more recent study, taking into account of high initial body burden, ongoing environmental exposure, low serum levels, and congeners with very long half-lives, has showed the estimated half-lives during a period of high internal dose were 1.74 years for Aroclor 1242 and 6.01 years for Aroclor 1254. Half-lives during a period of low internal dose were estimated to be 21.83 years and 133.33 years for Aroclor 1242 and Aroclor 1254, respectively [Hopf et al. 2013].

In general, less-chlorinated PCB congeners are more readily metabolized than are highly chlorinated congeners. As a result of this preferential metabolism, highly chlorinated congeners tend to remain in the body longer than do less-chlorinated congeners. Highly chlorinated congeners therefore tend to become more concentrated in adipose tissues, where they are stored in solubilized form.

Excretion

PCBs are primarily excreted after they have been conjugated and transformed into more polar metabolites. The major routes of excretion of PCBs are fecal and urinary.

Environmental Alteration of PCB Mixtures

Environmental PCBs occur as mixtures whose compositions differ from the commercial mixtures. This is because after release into the environment, PCB mixture composition changes over time through chemical transformation and preferential bioaccumulation [Cogliano 1998].

Chemical transformation can occur through biodegradation of PCB mixtures in the environment. PCBs with higher chlorine content are extremely resistant to oxidation and hydrolysis.

Preferential bioaccumulation occurs in living organisms. Bioaccumulation through the food chain tends to concentrate congeners of higher chlorine content. In humans, bioaccumulated PCBs also appear to be more persistent in the body [Hovinga et al. 1992]. This is significant because bioaccumulated PCBs appear to be more toxic than original Aroclors in animals [Aulerich et al. 1986; Cogliano 1998].

Key Points

- PCBs are stored in adipose tissues.
- The liver is the primary site of metabolism of PCBs.
- The slow metabolism and high lipid solubility of PCBs lead to bioaccumulation.
- Binding of PCB metabolites to nucleophilic cellular macromolecules may contribute to the toxic effects of PCBs.
- After release into the environment, PCBs occur as mixtures whose compositions differ from the commercial mixtures. Bioaccumulated PCBs also appear to be more persistent in the body.

Progress Check

6. Which of the following statements about the biologic fate of PCBs is **NOT CORRECT**?
- A. The liver is the primary site of PCBs metabolism, which occurs via hydroxylation and conjugation with glucuronic acid and sulfates.
 - B. Less-chlorinated congeners are more readily metabolized than are highly chlorinated congeners.
 - C. Highly chlorinated congeners tend to become more concentrated in muscle.
-

D. Bioaccumulated PCBs appear to be more persistent in the body.

To identify relevant content, see all topics in this section.

What Are Adverse Health Effects of PCB Exposure?

Learning Objective

Upon completion of this section, you will be able to

- Describe adverse health effects associated with exposure to PCBs.

Introduction

Human exposures to relatively high levels of PCBs have occurred primarily in persons working in plants that extensively manufactured and used PCBs and PCB-containing equipment. Occupational exposure to PCBs can result in a broad spectrum of effects that includes

- Increased levels of some liver enzymes, with possible hepatic damage,
- Chloracne and related dermal lesions, and
- Respiratory problems [Alvares et al. 1977; Chase et al. 1982; Emmett and Emmett 1985; Lawton et al. 1985; Meigs 1954; Ouw et al. 1976; Safe S 1993; Warshaw et al. 1979].

Potential adverse human health effects of low-level environmental exposure to PCBs are complex and still need further validation [Safe SH 2007].

In animal studies, commercial PCBs elicit a broad range of toxic responses including:

- Acute lethality,
 - Body weight loss,
 - Carcinogenesis,
 - Dermal toxicity,
 - Fatty liver,
 - Genotoxicity,
 - Hepatomegaly,
 - Immunosuppressive effects,
 - Neurotoxicity,
-

-
- Porphyria,
 - Reproductive and developmental toxicity,
 - Thymic atrophy, and
 - Thyroid hormone-level alterations.

This adverse health effects section addresses PCBs as a whole.

Mechanism of PCB Toxicity

PCBs are metabolized by the microsomal monooxygenase system catalyzed by cytochrome P-450 to phenols (via arene oxide intermediates), which can be conjugated or further hydroxylated to form a catechol. Arene oxide intermediates are electrophilic in nature. They can covalently bind to nucleophilic cellular macromolecules (e.g., protein, DNA, RNA) and induce DNA strand breaks and DNA repair, which can contribute to the toxic response of PCBs. Additionally, arene oxide intermediates can be conjugated with glutathione and further metabolized to form methylsulfonyl metabolites, which have been identified in human serum and tissue samples and in laboratory animals. Binding of methylsulfonyl metabolites to some proteins may contribute to some of the toxic effects of PCBs. It has also been hypothesized that hydroxylated PCB metabolites could contribute to the toxicity of PCBs [ATSDR 2000; Safe SH 2007].

Dermatologic Effects

Chloracne and related dermal lesions have been reported in workers occupationally exposed to PCBs. Mild to moderate chloracne was observed in 7 of 14 workers exposed to 0.1 mg/m³ Aroclors for an average duration of 14.3 months [Meigs 1954]. Among 80 workers who manufactured capacitors in Italy, 10 cases of acne or folliculitis, or both, and 5 cases of dermatitis were reported. All of the workers with chloracne were employed in high exposure jobs. Their blood PCB concentrations ranged from 41 to 1319 µg/kg [Maroni et al. 1981].

In a person with PCB-induced chloracne, the acne-like lesions arise as a result of inflammatory responses to irritants in the sebaceous glands. Chloracne usually begins with the formation of keratin plugs in the pilosebaceous orifices. The resulting inflammatory folliculitis stimulates keratinization of the sebaceous gland ducts and outer root sheath of the hair, leading to the formation of keratin cysts.

The chin, periorbital, and malar areas are most often involved, although lesions might also appear in areas not usually affected by acne vulgaris (e.g., the chest, arms, thighs, genitalia, and buttocks). The most distinctive lesions are cystic and measure 1–10 mm, although comedonal lesions can also be present. The cysts and comedones can become inflamed and secondarily infected, and papules and cysts can be surrounded by edema and erythema [Crow 1970; Letz 1983].

Chloracne generally indicates systemic toxicity and can be caused by not only dermal contact but also ingestion of PCBs. However, the absence of chloracne does not rule out exposure [Kimbrough 1980; Letz 1983]. No reliable dose-response model exists for chloracne in exposed populations, and the dose-response relationship might be dependent on individual predisposition. Chloracne typically develops weeks or months after exposure. The lesions are often refractory to treatment and can last for years or decades.

In addition to chloracne, other dermal effects noted in some PCB-exposed workers include pigmentation

disturbances of skin and nails, erythema and thickening of the skin, and burning sensations [Fischbein et al. 1982; Fischbein et al. 1979; Ouw et al. 1976; Smith et al. 1982].

Skin effects were reported widely among victims of the Yusho (Japan) and Yu-Cheng (Taiwan) poisoning episodes in 1968 and in 1978, respectively. In these episodes, persons were exposed to PCBs and their heat-degradation products, mainly polychlorinated dibenzofurans (PCDFs). Exposure to PCBs occurred by consuming rice oil that had become contaminated by heat-degraded PCBs during processing. Unlike usual PCB mixtures, the Yusho and Yu-Cheng mixtures were heated in thermal heat exchangers during the cooking process, resulting in contamination of the oil by chlorinated dibenzofurans as well as PCBs. This co-contamination created controversy [Anonymous 1997; Kimbrough et al. 2003; Ross 2004] about the extent to which the health effects observed in the Yusho and Yu-Cheng populations can be attributed to PCBs legitimately, as opposed to the dibenzofuran co-contaminants.

No adverse dermal effects have been reported in persons who consume large amounts of Great Lakes fish contaminated with PCBs and other environmentally persistent chemicals, or in other cohorts from the general population. However, whether this outcome was systematically studied in these cohorts is unknown [ATSDR 2000].

A skin lesion exactly like chloracne in humans has been observed in several species of animals experimentally exposed to PCBs [Allen 1975]. After monkeys incur long-term oral exposure to commercial PCB mixtures, related dermal effects are well characterized and generally are similar to those observed in humans [ATSDR 2000].

Key Points

- Conclusive evidence that exposure to PCBs induces adverse dermal effects in humans exists.
- A typical dermal sign of exposure is chloracne.

**Reproductive
and
Developmental
Effects**

Courval, DeHoog et al. [1999] conducted a study of 626 married couples in Michigan. The relative risk of conception failure (defined as inability to conceive after 12 months) rose in men but not in women with increasing consumption of PCB-contaminated fish. Some evidence shows that increased intake of PCB-contaminated fish can shorten menstrual cycle length, but no adverse association was found between the duration of fish consumption and time-to-pregnancy in the same population.

In a study of 1,820 multigravida women, no significant association was found between low-to-moderate PCB intake and clinically recognized spontaneous fetal death [Mendola et al. 1995].

A recent occupational cohort study examined the data from 2595 live births of female workers from three capacitor plants and found no evidence of altered sex ratio among children born to PCB-exposed female workers [Rocheleau et al. 2011].

The first epidemiologic investigation to demonstrate an association between the amounts of PCB-contaminated fish eaten by pregnant women and behavioral deficits in their newborns was the Michigan Maternal Infant Cohort Study, published in 1984 [Fein et al. 1984; Jacobson SW et al. 1985]. In this study, developmental and cognitive deficits were observed in the children of mothers who had eaten moderate to high amounts of contaminated fish during the six years preceding pregnancy and who continued to do so during pregnancy. Developmental effects in this population included statistically significant decreases in

- Gestational age (4.9 days),
- Birth weight (160–190 grams), and
- Head circumference (0.6 centimeters).

In addition, infants born to mothers who had eaten the greatest amount of contaminated fish during pregnancy exhibited weaker reflexes, greater motor immaturity, and more pronounced startle responses compared with infants

born to women who had consumed less fish.

It is essential that women of childbearing age be aware of fish advisories to ensure they not only limit their consumption of fish with elevated PCB levels but also learn how to prepare fish to limit their PCB ingestion.

Follow-up studies of the children from this cohort have demonstrated that the effects of perinatal exposure to PCBs are persistent. At four years of age, these children still had deficits in

- Weight gain,
- Depressed responsiveness, and
- Reduced performance on the visual recognition-memory test.

At 11 years of age, the children of highly exposed mothers were

- Three times more likely than controls to have low full-scale verbal IQ scores,
- Twice as likely to lag behind at least 2 years in reading comprehension, and
- More likely to have difficulty paying attention [Jacobson JL et al. 1990a, 1990b].

Recent studies indicate that maternal consumption of PCB-contaminated fish can cause disturbances in reproductive parameters and neurobehavioral and developmental deficits in newborns and older children. Prenatal exposure to PCBs from the mother's body burden, rather than exposure through human milk, is believed to account for the developmental effects of these compounds [Jacobson JL et al. 1996; Longnecker et al. 2003; Ribas-Fito et al. 2001; Schantz et al. 2003].

Similar reproductive, developmental, and neurobehavioral deficits have been reported in children born to women who were pregnant during the Yusho and Yu-Cheng incidents [Hsu et al. 2003; Hsu et al. 2005; Yang et al. 2005].

Developmental delays were seen at all ages and were

greater in children who were smaller and had neonatal signs of intoxication or nail deformities, or both. Follow-up testing indicated that effects on cognitive development persisted for several years after exposure [Guo et al. 1995].

In rhesus monkeys, exposure to PCBs is associated with alterations in the menstrual cycle, decreases in fertility, increases in spontaneous abortion, and a reduced number of conceptions [Arnold et al. 1990; Barsotti et al. 1976].

Key Points

- Reproductive function may be disrupted by exposure to PCBs.
- Neurobehavioral and developmental deficits have been reported in newborns exposed to PCBs in utero.

Endocrine Effects

Limited but corroborative occupational data indicate a potential for toxic effects in the thyroid system in humans. Studies that have examined relationships between exposure to PCBs and thyroid hormone status have reported a variety of results. Findings include both negative and positive significant correlations between exposure to PCBs and circulating levels of thyroid-stimulating hormone (TSH), T4, or T3. These findings are dependent on the:

- Specific type of analysis for exposure to PCBs,
- Age of the cohort, and
- Specific exposure scenario [Emmett et al. 1988; Koopman-Esseboom et al. 1994; Langer et al. 1998; Longnecker et al. 2003; Nagayama et al. 1998; Osius et al. 1999].

In a Dutch population, elevated levels of PCBs correlated with lower maternal levels of circulating triiodothyronine and total thyroxine and with higher plasma levels of TSH in infants during the second week and third month after birth. Infants exposed to higher levels of PCBs also had lower plasma levels of free thyroxine and total thyroxine in the second week after birth [Koopman-Esseboom et al. 1994].

In addition, a significantly elevated odds ratio for goiter was found among the Yu-Cheng cohort [Guo et al. 1999], suggesting the possibility of excessive thyroid disease in a population that experienced relatively high exposures to mixtures of PCBs and PCDFs.

Thyroid hormones are essential for normal behavioral, intellectual, and neurologic development. Thus, the deficits in learning, memory, and attention processes among the offspring of women exposed to PCBs are partially or predominantly mediated by alterations in hormonal binding to the thyroid hormone receptor [ATSDR and EPA 1998]. Some PCB congeners are capable of competing with endogenous hormone for binding to this receptor, suggesting a possible mechanism of thyroid toxicity. Hydroxylated PCB metabolites appear to be particularly potent in this regard [ATSDR 2000].

Studies in animals, including rodents and primates, provide evidence of thyroid hormone involvement in PCB toxicity. The most convincing evidence that PCBs can exert toxicity by disrupting thyroid hormone system derives from two studies in rats [Cooke et al. 1996; Goldey et al. 1998].

The contribution of persistent organic pollutants (POPs) exposure to the incidence of diabetes has received little attention until recently. Recent studies in populations exposed to PCBs and chlorinated pesticides found a dose-dependent elevated risk of diabetes [Carpenter 2008].

Key Points

- The epidemiological studies suggest a link between exposure to PCBs and thyroid hormone toxicity in humans.
- Studies in animals provide evidence of thyroid hormone involvement in the mechanism of PCB toxicity.

Hepatic Effects

Evidence for liver effects of occupational exposure to PCBs is essentially limited to elevation of serum liver enzymes that are routinely examined in clinical assays. These serum liver enzymes include aspartate aminotransferase (AST), alanine aminotransferase (ALT), glutamyl transpeptidase (GGT) and other biochemical indices (e.g., bilirubin). No overt hepatotoxicity has been

seen in workers exposed to PCBs [ATSDR 2000].

A cross-sectional survey found no significant differences in liver function test results between workers who manufacture capacitors with low-level chronic exposure and non-exposed controls [Fischbein et al. 1979]. However, in another cross-sectional study, liver function tests showed abnormalities that seemed to correlate with serum PCB levels [Maroni et al. 1981].

Increases in urinary excretion of porphyrins appear to be associated with occupational exposure to PCBs, an effect that is believed to be secondary to the induction of hepatic microsomal enzymes. Total bilirubin levels exhibit a positive correlation with serum PCB levels [Colombi et al. 1982; Maroni et al. 1984; Smith et al. 1982].

PCBs are more potent enzyme inducers than phenobarbital, a drug that occasionally causes clinical problems due to its microsomal enzyme-inducing effects. The health implications of enzyme induction include the occurrence of disease secondary to increased metabolism of endogenous or exogenous substances and interference in medical therapy due to increased metabolism of administered drugs. The enzyme-inducing effects of PCBs can persist long after cessation of exposure [Letz 1983].

In the Yu-Cheng population, the incidence of chronic liver disease and cirrhosis was significantly higher than the incidence of these conditions in the general population of Taiwan. Asymptomatic hepatomegaly has been reported in exposed workers, many of whom had concomitant elevated serum PCB levels. Due to the mixed chemical nature of the exposure, the results cannot be attributed solely to PCBs [ATSDR 2000].

Liver damage is a consistent and prominent finding among animals exposed to PCBs, particularly rats and monkeys, which are the species tested most extensively. Liver effects are similar in nature among species and appear to be reversible when mild. Liver effects characteristically include

- Fat deposition,

-
- Fibrosis,
 - Hepatic microsomal enzyme induction,
 - Increased serum levels of liver-related enzymes indicative of possible hepatocellular damages,
 - Liver enlargement, and
 - Necrosis [ATSDR 2000].

Key Points

- Although liver damage is common in animals exposed to PCBs, overt hepatotoxicity is uncommon in humans.
- Exposure to PCBs can increase serum levels of hepatic enzymes and can induce microsomal enzyme function.

Carcinogenic Effects

Epidemiologic studies have raised concerns about the potential carcinogenicity of PCBs.

A retrospective analysis of a study of two plants that manufactured electrical capacitors in the United States found a significant increase in the incidence of cancer. The primary target tissues for the cancers were the liver, gallbladder, and biliary tract [Brown 1987].

Likewise, an increased incidence of melanomas associated with exposure to PCBs has also been observed for workers who manufactured capacitors [Bahn et al. 1976; Ruder et al. 2006; Sinks et al. 1992]. Sinks et al. [1992] observed the increased risks for brain cancer among workers exposed to PCBs in an electrical capacitor manufacturing plant in Indiana, and this finding has been further confirmed by a recent study from Ruder et al. [2006].

One study suggests that exposure to electrical insulating fluids, for which the main constituent is PCBs, may cause malignant melanoma of the skin [Loomis et al. 1997].

The results of a mortality study of workers employed between 1944 and 1977 at an electrical capacitor manufacturing plant were recently reported. The report pointed out that PCBs alone or in combination with other chemicals could be associated with increased risks for

- Liver or biliary,
-

-
- Stomach, intestinal, and
 - Thyroid cancers [Mallin et al. 2004].

A recent analysis of a cohort of 24,865 capacitor-manufacturing workers exposed to PCBs at three plants showed evidence of associations between cumulative exposure to PCBs and increased total cancer and intestinal cancer mortality among female long-term workers and excess myeloma for male long-term workers [Ruder et al. 2014].

In contrast, increased cancer incidence was not observed in male workers who manufactured capacitors in Sweden exposed to PCBs for an average of 6.5 years [Gustavsson et al. 1986]. The results from the Swedish study, however, cannot rule out the possibility of a carcinogenic risk from PCB exposure because of the small size of the cohort and relatively brief follow-up period.

Different mixtures of PCBs had different potencies and, thus, different toxicity. As noted previously, PCB mixtures found in the environment are different from commercial PCB mixtures. EPA agreed that some mixtures of PCBs are more likely to cause cancer than others, and found that all PCBs mixtures can cause cancer [Cogliano 1998; EPA 1996c].

In environmental case-control studies that compared PCB concentrations in breast tissue in both women with (case patients) and without (case controls) breast cancer, some studies reported higher levels of total PCBs among case patients than control patients [Falck et al. 1992; Guttes et al. 1998; Wassermann et al. 1976]. Other studies found no elevated PCB levels in breast tissue in patients with breast cancer [Aronson et al. 2000; Liljegren et al. 1998; Unger et al. 1984]. A recent occupational cohort study found no overall elevation in breast cancer risk after occupational exposure to PCBs [Silver et al. 2009].

In persons without known occupational exposure to PCBs, elevations of PCB level in the adipose tissue and serum have been associated with an increased risk of non-Hodgkin lymphoma (NHL) [De Roos et al. 2005; Engel et al. 2007; Hardell E et al. 2001; Hardell L et al. 1996].

Rothman et al. 1997].

After registering as Yusho victims, 887 male and 874 female patients were observed for an average 11 years. A retrospective study found statistically significant increased liver cancer mortality rates among the males compared to national liver cancer mortality rates [Kuratsune et al. 1987].

A retrospective mortality study of 1940 Yu-Cheng cases found no statistically significant increased mortality from liver and intrahepatic bile duct cancers [Hsieh et al. 1996].

Before the comprehensive study conducted by Mayes et al. [1998], only commercial mixtures 60% chlorinated had been tested, and controversy existed about whether mixtures with lower chlorine content were carcinogenic. The Mayes et al. study [Mayes et al. 1998] supported the position that all PCB mixtures can cause cancer. Data from animal studies have shown that PCBs cause gastrointestinal tract tumors, hepatocarcinomas, leukemia, lymphomas, and pituitary tumors [ATSDR 2000].

On the basis of these laboratory data, EPA has determined that PCBs are probable human carcinogens and has assigned them the cancer weight-of-evidence classification B2 [IRIS 2012]. DHHS concluded that PCBs are reasonably anticipated to be carcinogenic in humans based on sufficient evidence of carcinogenicity in animals [NTP 2011].

In February 2013, 26 experts from 12 countries met at the International Agency for Research on Cancer (IARC), Lyon, France, to reassess the carcinogenicity of PCBs. The Working Group considered more than 70 independent epidemiological studies with informative data for carcinogenicity of PCBs in human beings. On the basis of sufficient evidence of carcinogenicity in humans and experimental animals, the IARC classified PCBs as carcinogenic to humans (Group 1). The classification is based on consistent association between exposure to PCBs and increased risk of melanoma in humans [IARC

2013].

Key Points

- On the basis of data from animal studies, DHHS and EPA consider PCBs a probable human carcinogen.
- On the basis of sufficient evidence of carcinogenicity in humans and experimental animals, the IARC classified PCBs as carcinogenic to humans (Group 1).

Other Effects

Occupational and epidemiologic studies have suggested or demonstrated other adverse health effects from exposure to PCBs. These health effects can involve the:

- Cardiovascular,
- Gastrointestinal,
- Immune,
- Musculoskeletal, and
- Neurological systems.

In southwest Quebec, adults who ate fish from PCB-contaminated waters had

- Significantly greater motor retardation,
- Poorer results on certain memory and attention tests, and
- Higher scores on a standardized confusion scale than did control adults.

These neurological deficits were directly related to the frequency of fish consumption [Mergler et al. 1998].

Immune system effects reported in PCB-exposed populations include alterations in the ratio of helper to killer (CD4+/CD8+) T-cells, decreases in IgA and IgM antibody levels, decreases in monocyte and granulocyte counts, and decreases in natural killer cell count [Svensson et al. 1994].

In the Yusho and Yu-Cheng populations, the immunosuppressive effects of PCB exposure were associated with an increased incidence of persistent respiratory infection and enhanced responsiveness to

mitogens [Guo et al. 1995].

Appetite loss has been reported in transformer and electrical equipment manufacturing workers exposed to various PCB-containing mixtures. Other nonspecific gastrointestinal symptoms experienced by workers exposed to PCBs include nausea, epigastric distress and pain, and intolerance to fatty foods [Emmett et al. 1988; Smith et al. 1982].

A recent study has indicated that several PCB metabolites induce gene mutations, chromosome breaks, chromosome loss and polyploidization in cells in culture and even provided the first evidence that a PCB congener is mutagenic in vivo [Robertson and Ludewig 2011].

Key Points

- Additional adverse effects of PCBs may involve the
 - Cardiovascular,
 - Gastrointestinal,
 - Genetic systems,
 - Immune,
 - Musculoskeletal, and
 - Neurological systems.

Progress Check 7. Adverse dermal effects have been reported in the following subjects **EXCEPT**

- A. Workers occupationally exposed to PCBs.
- B. Those in the general population who consume large amounts of fish contaminated with PCBs and other environmentally persistent chemicals.
- C. Victims of the Yusho (Japan) and Yu-Cheng (Taiwan) poisoning episodes exposed to PCBs and their heat-degradation products.
- D. Monkeys after long-term oral exposure to commercial mixtures of PCBs.

To identify relevant content, see "Dermal Effects" in this section.

8. Which of the following statements about the potential carcinogenicity of PCBs is considered **INCORRECT**?

- A. Potential human health effects from exposure to mixtures of PCBs do not include cancer.
- B. Some mixtures of PCBs are more likely to cause cancer than others.
- C. Exposure to PCBs has been associated with increased incidence of some cancers.
- D. Data from animal studies have shown clearly that PCBs cause different kinds of tumors.

To identify relevant content, see "Carcinogenic Effects" in this section.

9. Additional adverse effects of PCBs may include which of the following?

- A. Liver damage.
- B. Neurobehavioral and developmental deficits.
- C. Thyroid hormone anomalies.
- D. All of the above.

To identify relevant content, see "Other Effects" in this section.

Clinical Assessment

Learning Objective

Upon completion of this section, you will be able to

- Describe characteristic findings on clinical assessment of patients exposed to PCBs, and
 - Describe a rational approach for evaluating a patient with a history of occupational or environmental exposure, or both, to PCBs.
-

Introduction

Patients who have been exposed to PCBs often are undergoing clinical assessment long after their last exposure occurred (possibly years). The ability to extrapolate peak blood levels is problematic in these cases.

PCBs have low acute toxicity but are of public health concern because they persist in the environment, bioaccumulate in human and animal tissues, and potentially can cause chronic or delayed toxicity.

Documenting an adequate occupational and environmental exposure history in addition to a physical examination is essential for identifying health effects related to PCBs.

Identifying cases of chloracne may be helpful, but the absence of chloracne would not rule out significant exposure.

Patient History and Physical Examination

A detailed history will facilitate the diagnosis of chronic PCB poisoning. Pertinent information includes occupational histories of all household members and history of the patient's sport and subsistence fish consumption. Because PCBs are hepatotoxins, history of exposure to other potentially hepatotoxic agents, such as ethanol intake and medications with known hepatotoxicity, should be obtained.

During the physical examination, physicians should pay particular attention to the skin and hepatic systems. Encountering a patient with PCB toxicity should trigger consideration of whether this is a sentinel event, indicating the possibility of other similarly exposed

persons such as co-workers or family members.

**Signs and
Symptoms-
Acute
Exposure**

Acute exposure

PCBs have very low potential for producing acute toxic effects. The only overt sign of exposure to PCBs is chloracne, which is a specific skin lesion. Although chloracne may resemble typical adolescent acne, it has certain distinct features [Crow 1970; Letz 1983].

- Chloracne's most distinctive feature is cystic, skin colored lesions that measure 1–10 mm.
- Chloracne's other prominent feature is comedonal lesions.

The comedones and cysts can become inflamed and secondarily infected with large pustules.

Unlike adolescent acne, chloracne may occur at any age and may involve the arms, back, face, legs, neck, and trunk.

Chloracne can be very persistent and refractory to treatment.

Acneiform lesions do not appear in all severely exposed patients, so the absence of chloracne does not rule out exposure. New cases of chloracne should be reported to the local or state health department.

Other acute effects that may be seen include eye irritation, nausea, and vomiting [LaDou 2006].

Elevated liver enzymes are the most sensitive indicator of exposure to PCBs in animals, and alterations in

- AST (SGOT),
- GGT (GGTP),
- Bilirubin, and
- Albumin levels have been reported in human epidemiologic studies.

The absence of alterations in these liver function markers does not rule out excessive exposure to PCBs.

The presence of specific signs, symptoms, or laboratory abnormalities, with the possible exception of chloracne, is difficult to relate to exposure to PCBs absolutely in any given patient. A practical approach for the routine work-up of individual patients potentially exposed to PCBs would be to do the following:

- Take a thorough occupational and environmental exposure history,
- Examine the skin,
- Order baseline liver function tests, and
- If indicated, perform subsequent testing limited to patients with clinical problems or history of extensive exposure such as an accidental spill or a capacitor rupture that caused heavy skin contamination [Letz 1983].

This clinical approach may be used for monitoring electrical utility workers or other persons with some potential for ongoing occupational exposure.

Serum PCB level is a useful indicator of a patient's exposure. Serum PCB tests are readily available at most commercial reference laboratories. However, serum PCB levels may not be consistent with adverse health effects. [Roseman 2005].

**Signs and Symptoms-
Chronic
Exposure**

Chronic exposure

Many people who are chronically exposed to PCBs exhibit no overt signs or symptoms of toxicity. Among persons with hepatic involvement, signs of exposure to PCBs can include

- Abdominal pain,
 - Anorexia,
 - Jaundice,
 - Nausea,
 - Vomiting,
 - Weight loss, and
-

-
- Uroporphyrin.

Headache, dizziness, and edema have also been reported (see earlier section on Adverse Health Effects for more detail).

Differential Diagnosis

Occupational exposure to PCBs may be accompanied by exposure to chlorinated dibenzodioxin and dibenzofuran contaminants, which are much more toxic than PCBs in comparative animal studies. These substances can cause chronic fatigue and elevated liver enzymes.

Mild chloracne should not be confused with other rashes (e.g., acne, seborrheic keratitis, keratoma). A skin biopsy of lesions may help establish the diagnosis [LaDou 2006].

Medical Surveillance

Workers intermittently exposed to PCBs should have a baseline skin examination and liver function tests. Follow-up examination can be limited to symptomatic persons and workers exposed as a consequence of accidental contamination. For persons with signs and symptoms consistent with high exposures to PCBs (e.g., chloracne, elevated AST and ALT), a serum PCB level should be obtained to confirm exposure.

Key Points

- Chloracne is the only known overt sign of PCB toxicity; however, the absence of chloracne does not rule out exposure.
- Signs of low level, chronic exposure to PCBs are generally subtle, if present at all.

Progress Check

10. Which of the following should be included in the clinical evaluation of a patient with a history of exposure to PCBs?
- A. A thorough occupational and environmental exposure history.
 - B. A thorough skin examination.
 - C. Liver function tests.
 - D. All of the above.

To review relevant content, see "Patient History and Physical Examinations" in this section.

11. PCB exposure may manifest clinically as which of the following?

- A. Acne vulgaris.
- B. Chloracne.
- C. Parkinsonism.
- D. Acute tubular necrosis.

To review relevant content, see "Signs and Symptoms – Acute Exposure" and "Signs and Symptoms – Chronic Exposure" in this section.

Clinical Assessment - Laboratory Tests

Learning Objective

Upon completion of this section, you will be able to

- Describe measurements that can help diagnose exposure to PCBs.
-

Introduction

The lipophilic nature of PCBs causes them to accumulate in fat; consequently, analyzing biopsied adipose tissue has been used to measure long-term exposure.

Serum PCB analysis is less invasive than tissue biopsy, and it can be performed by most commercial reference laboratories. Although such tests are useful for gauging exposure, they may not be consistent with adverse health effects.

Select laboratories have the capability to perform PCB analyses on human tissue. Testing human tissue for PCB content, however, remains principally a research tool.

Direct Biologic Indicators

PCBs have been detected in the blood, adipose tissue, and breast milk of non-occupationally exposed members of the general population [CDC 2009; EPA 1986b; Greizerstein et al. 1999; Gunderson and Gunderson 1995; Patterson et al. 2008]. Since the United States stopped making PCB compounds, body burdens of PCBs in humans have decreased. This decrease is evidenced by lower PCB levels reported in human adipose tissue, blood serum, and breast milk [Anderson et al. 1998; Fensterheim 1993; Hanrahan et al. 1999; Lunden et al.

1998; Schade et al. 1998].

PCB compounds generally can be found at the parts per trillion (ppt) levels in the lipid stores of humans, especially persons living in industrialized societies. The general population is exposed to PCB compounds primarily by ingesting high-fat foods, such as

- Dairy products,
- Eggs,
- Animal fats, and
- Some fish and wildlife [CDC 2009; Patterson et al. 2008].

However, no specified PCB values are deemed normal or toxic levels.

Some researchers believe that PCB levels in the serum and tissue provide a reliable measurement of long-term exposure. PCB levels in the serum and tissue can be measured by many laboratories although analyses results may not be consistent with health effects.

A correlation between increasing levels of serum PCBs and dermatologic findings, including chloracne, has not been found consistently in human epidemiologic studies. However, statistically significant associations between dermatologic effects and plasma levels of higher chlorinated PCB congeners have been reported [Fischbein et al. 1982; Fischbein et al. 1979; Smith et al. 1982].

Although PCBs accumulate in breast milk, the American Association of Pediatrics (AAP) has concluded that the risks posed by PCBs in breast milk are outweighed by the benefits of breastfeeding in all but the most unusual circumstances. Therefore, AAP does not recommend that breast milk be tested for PCBs because the test results would not likely change the recommendation to breast feed. Additionally, AAP recommends consulting local health department officials who are aware of the PCB problems in unusual circumstances or where high exposures have occurred [AAP 2003].

**Indirect
Biologic
Indicators**

Liver function tests are nonspecific.

The combination of asymptomatic hepatomegaly and mild, nonspecific elevations of hepatic enzymes suggests a chronic inflammatory liver process or hepatitis.

Hepatitis can be

- Drug-induced,
- Genetic,
- Infectious,
- Toxic,
- Caused by ethanol ingestion, or
- Associated with connective tissue disease.

The major cause of liver disease in the United States is ethanol ingestion. Less common causes are environmental exposures, resulting in either acute or chronic toxic hepatitis.

Infectious hepatitis includes disease caused by viruses such as A, B, C, and other possible agents of non-A, non-B hepatitis. Hepatitis can also occur with Epstein-Barr virus and cytomegalovirus infections. Some connective tissue diseases such as lupus erythematosus are associated with a specific type of hepatitis. Infiltrative diseases such as sarcoidosis or amyloidosis, and rare genetic diseases such as Wilson disease, primary hemochromatosis, and alpha-1-antitrypsin deficiency, must be excluded.

Normal liver enzyme values do not rule out significant PCB exposure; body burden still might be elevated.

To help arrive at a diagnosis, viral serology and a heterophil antibody test should be considered. If the patient has suggestive signs or symptoms, a serum iron and total iron binding capacity, serum copper and ceruloplasmin, and antinuclear antibodies might help with the diagnosis. Assays for suspected hepatotoxins might also be useful. If other tests do not provide sufficient information, further evaluation might include ultrasound and percutaneous liver biopsy.

Key Points

- Serum or adipose tissue PCB levels can indicate exposure, but they are difficult to interpret clinically.
- AAP does not recommend testing breast milk for PCBs, and encourages breastfeeding in all but the most unusual circumstances.
- Elevated hepatic enzyme levels are of limited value in diagnosing exposure to PCBs.

Progress Check 12. Which of the following statements is true?

- A. Testing PCB serum level is expensive and not readily available, but correlates well with health risk.
- B. AAP recommends that breast milk be tested for PCBs because human milk contains a steroid that inhibits PCB metabolism and excretion.
- C. The toxic serum PCB value is >20 ppb.
- D. None of the above.

To review relevant content, see "Direct Biologic Indicators" in this section.

How Should Patients Exposed to PCBs Be Treated and Managed?

Learning Objectives

Upon completion of this section, you will be able to

- Describe the principal treatment strategy for managing PCB poisoning and
- Describe the measures for preventing occupational and environmental exposure to PCBs.

Introduction

No specific treatment exists for PCB accumulation. Patients should avoid further PCB exposure and also avoid other hepatotoxic substances, including ethanol.

Acute Exposure	<p>Treat acute skin and eye PCB exposure immediately by flushing with copious amounts of water. However, post-contamination washing cannot ensure removal of all contamination [Wester et al. 1983].</p> <p>Remove contaminated clothing and discard properly.</p> <p>Carefully observe patients with inhalation exposure for any systemic signs or symptoms of toxicity and administer treatment as necessary. No specific measures are available to reduce respiratory tract absorption.</p> <p>In the rare event of ingestion of PCBs, emesis would be contraindicated because of the high risk of aspiration. The value of administering activated charcoal after ingestion is unknown. Unless a patient has an intact or protected airway, administering charcoal is contraindicated [Alaspaa et al. 2005; Chyka et al. 2005].</p> <p>Exposed persons should have periodic follow-up examinations with particular attention to hepatic function and dermal lesions.</p>
Key Points	<ul style="list-style-type: none"> • No antidote exists for PCB exposure; therefore, treatment is supportive.
Chronic Exposure	<p>No specific treatment is available for chronic PCB toxicity. Because no known methods exist for reducing the reserves of PCBs in adipose tissues, purging the body of PCBs should not be attempted.</p> <p>Initial treatment of chloracne is based on</p> <ul style="list-style-type: none"> • Cessation of PCB exposure, • Good skin hygiene, and • Dermatologic measures commonly used for acne vulgaris. <p>Given the difficulty in treating chloracne, the patient should be referred to a dermatologist.</p> <p>If chronic exposure has occurred due to consuming contaminated fish or game, the patient should be</p>

informed that PCBs tend to accumulate in the body with continued exposure, and counseled about the importance of minimizing further exposure.

In areas with a known PCB problem, state and local public health or natural resources departments typically issue advisories. These advisories specify the waters or hunting areas where PCB-contaminated fish and game likely are, and list the species and size of fish or game that are of concern. Such advisories might completely ban consumption, or might recommend limits on the frequency with which certain species are to be consumed. To minimize the risk for further exposure, sport and subsistence fishers are encouraged to familiarize themselves with and observe advisory recommendations [ATSDR 2000].

Patients should be monitored for increased hepatic enzymes. Because PCBs are hepatotoxins, history of exposure to other potentially hepatotoxic agents should be obtained. To minimize the risk of hepatic damage, patients should be encouraged to avoid exposure to other hepatotoxins, including medications with known hepatotoxicity, ethanol, and chlorinated solvents.

The carcinogenic potential and other risks from exposure to PCBs should be carefully reviewed with the patient.

AAP encourages breastfeeding in all but the most unusual circumstances [AAP 2003].

**Prevention in
the Workplace****Work Practices**

The following measures [LaDou 2006] may be adopted at work to avoid exposure to PCBs.

- Eliminate PCBs from the workplace or implement engineering changes to isolate the PCBs. If neither of these approaches is feasible, then use special PCB-resistant gloves and protective clothing.
- Maintain adequate ventilation during spill cleanup or maintenance of vessels containing PCBs. If this is not possible, provide approved respirators.
- Make provisions for proper decontamination or disposal of contaminated clothing or equipment.
- Post clearly the locations where PCBs are stored as required by law.
- Conduct environmental sampling as necessary to ensure adequate worker protection or safety for public reentry to contaminated areas.
- Establish reentry or cleanup levels for dioxins and PCBs to protect workers who reoccupy buildings after a PCB fire.
- Record health complaints of any type.

Medical Surveillance

Workers intermittently exposed to PCBs should have a baseline skin examination and liver function tests. For workers with signs and symptoms consistent with large exposures to PCBs (e.g., chloracne, elevated AST and ALT), obtain confirmation of exposure to determine serum PCB level.

**Prevention at
Home****Home Practices**

- Open all windows and use fans in your workspace when maintaining or repairing any products containing PCBs.
 - Wear a respirator or protective gloves, or both.
 - You and your children may be exposed to PCBs by eating fish or wildlife caught from contaminated locations. Certain states, Native American tribes, and U.S. territories have issued advisories to warn people about PCB-contaminated fish and fish-eating
-

wildlife. You can reduce your family's exposure to PCBs by following these advisories.

Key Points

- The goal of treating chronically exposed patients is preventing any additional exposure to PCBs.
 - Exposure to PCBs at work or home is avoidable if the proper preventive measures are adopted.
-

Progress Check

13. Which of the following statements regarding treatment for chronic PCB toxicity is **NOT CORRECT**?
- A. The goal in treating chronically exposed patients is preventing any additional exposure to PCBs.
 - B. No specific treatment is available for chronic PCB toxicity.
 - C. Breastfeeding should be avoided.
 - D. No known methods exist for reducing the burdens of PCBs in human tissues.

To review relevant content, see "Chronic Exposure" in this section.

14. All of the following preventive measures to avoid PCB exposure at work or home are true **EXCEPT**
- A. Use special PCB-resistant gloves and protective clothing.
 - B. Maintain adequate ventilation during spill cleanup or maintenance of vessels containing PCBs. If this is not possible, provide masks.
 - C. Certain states, Native American tribes, and U.S. territories have issued advisories to warn people about PCB-contaminated fish and fish-eating wildlife. You can reduce your family's exposure to PCBs by obeying these advisories.
 - D. Locations where PCBs are stored should be clearly posted as required by law.

To review relevant content, see "Prevention at Home" and "Prevention in the Workplace" in this section.

What Instructions Should Be Given to Patients Exposed to PCBs?

Learning Objective

Upon completion of this section, you will be able to

- Describe appropriate instructions for patients exposed to PCBs.

Introduction

All patients exposed to PCBs 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.

ATSDR has developed a patient education sheet on PCBs that you might find useful. It can be found at http://www.atsdr.cdc.gov/csem/pcb/docs/pcb_patient_education.pdf

Self Care Guidance for Patients

Patients should be advised to avoid exposures and conditions that might further increase their risk of disease or worsen their existing condition.

At Work

- Eliminate PCBs from the workplace, or implement engineering changes to isolate the PCBs. If neither of these approaches is feasible, use special PCB-resistant gloves and protective clothing.
 - Maintain adequate ventilation during spill cleanup or maintenance of vessels containing PCBs. If this is not possible, provide approved respirators.
 - Make provisions for proper decontamination or disposal of contaminated clothing or equipment.
 - Dispose of existing PCBs through appropriate toxic waste facilities.
 - Conduct environmental sampling as necessary to ensure adequate worker protection or safety for public reentry to contaminated areas.
 - Establish reentry or cleanup levels for dioxins and PCBs to protect workers who reoccupy buildings after a PCB fire.
-

-
- Report persistent health effects (e.g., unexplained weight loss, muscle pain, frequent coughing, and sleep problems). These symptoms may be due to stress or recall bias and may not be specifically linked to the toxic effects of PCBs.

At Home

- Open all windows and use fans in your workspace when conducting maintenance or repairing any products containing PCBs.
- If ventilation is poor, wear a respirator and protective gloves.
- Seek medical attention immediately if an acute exposure occurs.
- Lower exposure to PCBs by looking for and following health advisories issued by states, Native American tribes, or U.S. territories when eating fish or wildlife caught from locations contaminated with PCBs.

Clinical Follow- up Guidance for Patients

PCBs have been implicated as a potential cause of cancer in humans. Screening tests are available for breast cancer and melanoma. If patients believe that they are being exposed to PCBs, advise them how to stop the exposure. Also tell them how to contact worksite or environmental regulatory agencies that will assess exposure risks and prescribe protective actions.

Advise patients with suspected or confirmed historic exposure to PCBs to be seen by you or their primary care provider periodically and monitored for signs of disease and changes in health status.

Advise patients to consult their physicians if they develop signs or symptoms of PCB exposure such as

- Appetite loss,
- Joint pain,
- Nausea,
- Skin disorders, changes, or discoloration,
- Breast changes or lumps, and/or
- Stomach distress and pain.

ATSDR's patient education sheet on PCBs includes a more

detailed checklist that you can use to indicate which types of follow up are relevant for a given patient.

Key Points

- Advise patients to avoid PCB exposures and conditions that might further increase their risk of disease or worsen their existing condition.
 - Advise patients to contact their physicians if they develop skin problems or other health changes.
-

Progress Check

15. Patients who have been exposed to PCBs should be advised to
- A. Speak to their employers about reducing workplace exposures (if exposures are occupational).
 - B. Learn how to avoid further exposure.
 - C. Know when to call their doctors.
 - D. All of the above.

To review relevant content, see all topics in this section.

Sources of Additional Information

Polychlorinated Biphenyls (PCBs) Specific Information

Please refer to the following resources for more information on the adverse effects of PCBs, the treatment of PCB-associated diseases, and management of persons exposed to PCBs.

- ATSDR <http://www.atsdr.cdc.gov>
 - For chemical emergency situations, contact
 - CDC Emergency Response at 770-488-7100 and request the ATSDR Duty Officer
 - For chemical non-emergency situations, contact
 - CDC-INFO at <http://www.cdc.gov/cdc-info/>
 - 800-CDC-INFO at (800-232-4636) TTY 888-232-6348 - 24 Hours/Day
 - E-mail at: cdcinfo@cdc.gov

PLEASE NOTE

ATSDR cannot respond to public inquiry and questions about individual medical cases, provide second opinions, or make specific recommendations regarding therapy. Such guidance requires clinical examination by a health care provider.

- Toxicological Profile for Polychlorinated Biphenyls (PCBs)
<http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=142&tid=26>
- Addendum to the Toxicological Profile for Polychlorinated Biphenyls (PCBs)
http://www.atsdr.cdc.gov/toxprofiles/pcbs_addendum.pdf
- TOXFAQs for Polychlorinated Biphenyls (PCBs) (English)
<http://www.atsdr.cdc.gov/toxfaqs/tf.asp?id=140&tid=26>
- TOXFAQs for Polychlorinated Biphenyls (PCBs) (Spanish)
http://www.atsdr.cdc.gov/es/toxfaqs/es_tfacts17.html
- ATSDR Minimal Response Levels
<http://www.atsdr.cdc.gov/mrls/index.html>
- Centers for Disease Control and Prevention
<http://www.cdc.gov>
- EPA Polychlorinated Biphenyls (PCBs)
<http://www.epa.gov/epaoswer/hazwaste/pcbs/index.htm>

General Environmental Health Information

Please refer to the following Web resources for general information on environmental health.

- ATSDR <http://www.atsdr.cdc.gov>
 - Taking an Exposure History CSEM
<http://www.atsdr.cdc.gov/csem/csem.asp?csem=17&po=0>
 - View the complete library of CSEMs
<http://www.atsdr.cdc.gov/csem/csem.html>
-

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- Exposure History Worksheet
<http://www.atsdr.cdc.gov/csem/csem.asp?csem=17&po=19>
 - ATSDR Regional Operations.
 - ATSDR regional staff are able to maintain current and historic knowledge of the sites and issues in their regions through the working relationships they have established with EPA, other federal and state agencies, individual citizens, and community groups.
 - A list of ATSDR's regional staff, the states and territories that they cover, and contact information can be found at http://www.atsdr.cdc.gov/DRO/dro_contact.html
 - ATSDR State Cooperative Agreement Program
<http://www.atsdr.cdc.gov/states/index.html>
 - The Cooperative Agreement Program provides essential support to communities nationwide to fulfill the mission of ATSDR.
 - The program funds ~30 states and one tribal government to help develop and strengthen their abilities to evaluate and respond to environmental public health issues.
 - CDC <http://www.cdc.gov>
 - CDC works to protect public health and safety by providing information to enhance health decisions, and promotes health through partnerships with state health departments and other organizations.
 - CDC focuses national attention on developing and applying activities surrounding disease prevention and control (especially infectious diseases), environmental health, occupational safety and health, health promotion, and education designed to improve the health of the people of the United States.
 - National Center for Environmental Health (NCEH)
-

<http://www.cdc.gov/nceh>

- NCEH works to prevent illness, disability, and death caused by interactions between people and the environment. NCEH is especially committed to safeguarding the health of populations that are particularly vulnerable to certain environmental hazards—children, the elderly, and people with disabilities.
 - NCEH seeks to achieve its mission through science, service, and leadership.
 - National Institute of Health (NIH)
<http://www.nih.gov>
 - A part of the U.S. Department of Health and Human Services, NIH is the primary federal agency for conducting and supporting medical research.
 - National Institute for Occupational Safety and Health (NIOSH) <http://www.cdc.gov/niosh/>
 - NIOSH is part of the U.S. Department of Health and Human Services and is an agency established to help ensure safe and healthful working conditions for working men and women by providing research, information, education, and training in the field of occupational safety and health.
 - American College of Occupational and Environmental Medicine (ACOEM) <http://www.acoem.org/>
 - ACOEM is the nation's largest medical society dedicated to promoting the health of workers through preventive medicine, clinical care, research, and education.
 - ACOEM members are a dynamic group of physicians including specialists in a variety of medical practices. ACOEM is united to develop positions and policies on vital issues relevant to preventive medicine both within and outside of
-

the workplace.

- American College of Medical Toxicologists (ACMT) <http://www.acmt.net>
 - ACMT is a professional, nonprofit association of physicians with recognized expertise in medical toxicology.
 - ACMT is dedicated to advancing the science and practice of medical toxicology through a variety of activities.

 - American College of Preventive Medicine (ACPM) <http://www.acpm.org>
 - ACPM is the national professional society for physicians committed to disease prevention and health promotion.
 - ACPM's 2,000 members are engaged in preventive medicine practice, teaching, and research.

 - Association of Occupational and Environmental Clinics (AOEC) <http://aoec.org>
 - AOEC is a network of more than 60 clinics and more than 250 individuals committed to improving the practice of occupational and environmental medicine through information sharing and collaborative research.

 - Pediatric Environmental Health Specialty Units (PEHSUs) <http://www.aoec.org/PEHSU.htm>
 - Based at an academic center, each PEHSU is a collaboration between the pediatric clinic and the AOEC occupational and environmental clinic at that site.
 - PEHSUs have been developed to provide education and consultation for health professionals, public health professionals, and other providers about the topic of children's environmental health.
 - PEHSU staff are available for consultation about
-

potential pediatric environmental health concerns affecting both the child and the family. Health care professionals may contact their regional PEHSU site for clinical advice.

- Poison Control Center
 - The American Association of Poison Control Centers (AAPC) may be contacted for questions about poisons and poisonings. Their Web site provides information about poison centers and poison prevention. AAPC does not provide information about treatment or diagnosis of poisoning, or research information for student papers.
 - American Association of Poison Control Centers may be contacted at 1-800-222-1222 or <http://www.aapcc.org>

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Table of Tables and Figures

Table	Title
1.	Standards, regulations, and recommendations for PCBs

Figure	Title
1.	Polychlorinated Biphenyls (PCBs)
