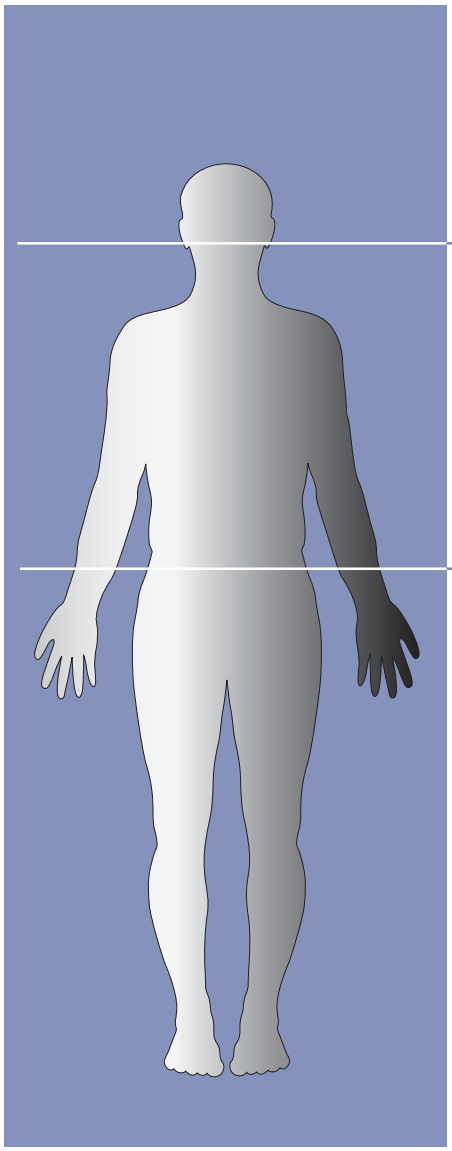
ATSDR
AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY

Case Studies in Environmental Medicine

Course: SS3067
Revision Date: September 2000
Original Date: June 1990
Expiration Date: September 30, 2006



POLYCHLORINATED BIPHENYLS (PCB) TOXICITY

Environmental Alert

- PCBs cause cancer in animals and are probably carcinogenic in humans (group 2A classification, International Agency for Research on Cancer).
- Recent evidence suggests that PCBs might also have adverse reproductive, developmental, and endocrine effects.
- The manufacture of PCBs has been banned since 1977.
- The highest human exposures to these compounds occur via the consumption of contaminated fish and in certain occupational setting via contact with pre-1977 equipment.
- The most common signs of exposure to PCBs are chloracne and elevation of liver enzymes.

This monograph is one in a series of self-instructional publications designed to increase the primary care provider's knowledge of hazardous substances in the environment and to aid in the evaluation of potentially exposed patients. This course is also available on the ATSDR Web site, www.atsdr.cdc.gov/HEC/CSEM/. See page 3 for more information about continuing medical education credits, continuing nursing education units, and continuing education units.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Agency for Toxic Substances and Disease Registry
Division of Toxicology and Environmental Medicine

ATSDR/DHEP Authors: Kimberly Gehle, MD, MPH; Darlene Johnson, RN, BSN, MA; Felicia Pharagood-Wade, MD, FACEP; Lourdes Rosales-Guevara, MD

ATSDR/DHEP Case Studies Team: Diane Dennis-Flagler, MPH; Sharon Hall, RN, PhD (CDC/PHPPO); Kimberly Gehle, MD, MPH; Felicia Pharagood-Wade, MD, FACEP

Edited By: Pamela S. Wigington

Original Contributors: Roger Wabeke, CIH; Richard Weinstein, MD, MPH

Peer Reviewers: Charles Becker, MD; Jonathan Borak, MD; Joseph Cannella, MD; Robert Fried, MD; Bernard Goldstein, MD; Alan Hall, MD; Richard J. Jackson, MD, MPH; Jonathan Rodnick, MD; Robert Wheater, MS; Brian A. Wummer, MD

The state of knowledge regarding the treatment of patients potentially exposed to hazardous substances in the environment is constantly evolving and is often uncertain. In this monograph, ATSDR has made diligent effort to ensure the accuracy and currency of the information presented, but makes no claim that the document comprehensively addresses all possible situations related pediatrics and environmental health. This monograph is intended as a resource for pediatricians and other child health care providers in assessing the condition and managing the treatment of patients potentially exposed to hazardous substances. It is not, however, a substitute for the professional judgment of a health care provider. The document must be interpreted in light of specific information regarding the patient and in conjunction with other sources of authority.

Use of trade names and commercial sources is for identification only and does not imply endorsement by the Agency for Toxic Substances and Disease Registry or the U.S. Department of Health and Human Services.

Table of Contents

Figures and Tables

Each content expert for this case study indicated no conflict of interest to disclose with the case study subject matter.

ATSDR Publication No.: ATSDR-HE-CS-2003-0001

Case Studies in Environmental Medicine (CSEM): PCB Toxicity

Goals and Objectives

The goals of this CSEM are to increase the knowledge of health care providers, especially pediatricians, of the special susceptibilities of children to hazardous substances in the environment and to aid in their evaluation of potentially exposed patients.

After completion of this educational activity, the reader should be able to discuss the major route of exposure for PCBs, describe two potential environmental and occupational sources of PCB exposure, give two reasons why PCBs are a health hazard, describe three factors contributing to PCB toxicity, identify evaluation and treatment protocols for persons exposed to PCBs, and list two sources of information on PCBs.

Accreditation

Continuing Medical Education (CME)

The Centers for Disease Control and Prevention (CDC) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. CDC designates this educational activity for a maximum of 1.0 hours in category 1 credit toward the American Medical Association (AMA) Physician's Recognition Award. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

Continuing Nursing Education (CNE)

This activity for 1.5 contact hours is provided by CDC, which is accredited as a provider of continuing education in nursing by the American Nurses Credentialing Center's Commission on Accreditation.

Continuing Education Units (CEU)

CDC has been approved as an Authorized Provider of continuing education and training programs by the International Association for Continuing Education and Training and awards 0.1 continuing education units (CEUs).

Instructions

See page 4

The questionnaire and posttest must be completed and returned electronically, by fax, or by mail for eligibility to receive continuing education credit.

Instructions for Completing CSEM Online

1. Read this CSEM, *Polychlorinated Biphenyl (PCB) Toxicity*; all answers are in the text.
2. Link to the MMWR/ATSDR Continuing Education General Information page (www.cdc.gov/atsdr/index.html).
3. Once you access this page, select the Continuing Education Opportunities link.
4. Once you access the MMWR/ATSDR site online system, select the electronic file and/or register and test for a particular ATSDR course.
   a. Under the heading "Register and Take Exam," click on the test type desired.
   b. If you have registered in this system before, please use the same login and password. This will ensure an accurate transcript.
   c. If you have not previously registered in this system, please provide the registration information requested. This allows accurate tracking for credit purposes. Please review the CDC Privacy Notice (www.cdc.gov/privacy.htm).
   d. Once you have logged in/registered, select the test and take the posttest.
5. Answer the questions presented. To receive continuing education credit, you must answer all of the questions. Some questions have more than one answer. Questions with more than one answer will instruct you to "indicate all that are true."
6. Complete the course evaluation and posttest no later than September 29, 2006.
7. You will be able to immediately print your continuing education certificate from your personal transcript.

Instructions for Completing CSEM On Paper

1. Read this CSEM, *Polychlorinated Biphenyl (PCB) Toxicity*; all answers are in the text.
2. Complete the evaluation questionnaire and posttest, including your name, mailing address, phone number, and e-mail address, if available.
3. Circle your answers to the questions. To receive your continuing education credit, you must answer all of the questions.
4. Sign and date the posttest.
5. Return the evaluation questionnaire and posttest, no later than September 1, 2006, to CDC by mail or fax:

Mail	**or**	**Fax**
Continuing Education Coordinator Division of Toxicology and Environmetnal Medicine, ATSDR 1600 Clifton Road, NE (MS F-32) Atlanta, GA 30333		770-488-4178 ATTN: Continuing Education Coordinator

6. You will receive an award certificate within 90 days of submitting your credit forms. No fees are charged for participating in this continuing education activity.

Case Study

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 office for a follow-up appointment. You first saw this patient about 3 weeks ago. At that time, he had multiple acneform 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 used over-the-counter astringents and antiacne medications, but they did not affect the lesions.

A review of the patient's medical history indicates that he has Gilbert syndrome and occasionally had elevated bilirubin levels in the past. However, the patient has no history of hepatitis, contact with hepatitis patients, other liver difficulties, or blood transfusion. There is no family history of cardiovascular disease or cancer. The patient does not smoke; he drinks 2 to 3 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 with 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 last year. He spends a lot of time in the basement area, which includes a workshop, recreation room with pool table, and laundry and heating facilities. An avid fisherman, he spends most weekends fishing in Lake Michigan and eating his catch with his two sons.

At the end of the patient's previous visit, you prescribed a topical antibiotic and instructed the patient on its use. After reassuring the patient that stronger prescription medications are available for the treatment of acne, you ordered a serum biochemical and hematologic profile to document baseline values in the event that a course of Accutane (isotretinoin) therapy is warranted.

During today's physical examination, you note little or no improvement in the patient's acne. The ratio of cystic to comedome lesions seems 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 appear to be developing areas of folliculitis on his chest and forearms.

In addition to this worsening of the patient's symptoms of acne, physical examination reveals mild, nontender hepatomegaly without jaundice. This finding causes you to review the results of the biochemical panel, and you are surprised to 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 230 IU/L (normal 50–225).

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

Pretest

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

(b) What is a differential diagnosis for the patient's altered liver enzymes?

(c) What tests would be useful in helping you arrive at a diagnosis?

Exposure Pathways

PCBs are the family of chemicals formed by attaching one or more chlorine atoms to a pair of connected benzene rings (Figure 1). Depending on the number and position of chlorine atoms attached to the biphenyl ring structure, 209 different PCB congeners can be formed. The chemical and toxicologic properties of PCBs vary from one congener to the next.

Because of their insulating and nonflammable properties, PCBs were marketed for nearly 40 years (ATSDR 2000a) as heat exchange and dielectric fluids in transformers and capacitors; hydraulic and lubricating fluids; diffusion pump oils; plasticizers; extenders for pesticides; and as ingredients in caulking compounds, paints, adhesives, and flame retardants. PCBs have also been used in inks and carbonless carbon paper. Commercial PCB products were always mixtures of different PCB congeners and were usually contaminated with small amounts of

polychlorinated dibenzofurans (furans) or polychlorinated dibenzodioxins (dioxins). Contamination is a concern because the toxicity of contaminants is generally much greater than that of PCBs. Trade names for commercial PCB mixtures included Aroclor, Askarel, Eucarel, Pyranol, Dykanol, Clorphen, Asbestol, Diaclor, Nepolin, and EEC-18.

No known natural sources of PCBs exist. Production of these chemicals was banned in 1977, when their ability to accumulate in the environment and to cause harmful effects became apparent (ATSDR 2000a). Today, the major source of ambient PCB exposure seems to be environmental cycling of PCBs previously released into the environment. Of the 1.25 billion pounds of PCBs produced in this country between 1929 and 1977, about 450 million pounds have found their way into the environment. PCBs can be released into the general environment from poorly maintained toxic waste sites; by illegal or improper dumping of PCB wastes, such as transformer fluids; through leaks or fugitive emissions from electrical transformers containing PCBs; and by disposal of PCB-containing consumer products in municipal landfills. PCBs have been found in at least 432 of the 1,467 hazardous waste sites on the U.S. Environmental Protection Agency (EPA) National Priorities List (NPL) (ATSDR 2000a), and low levels of PCBs can be found throughout the world.

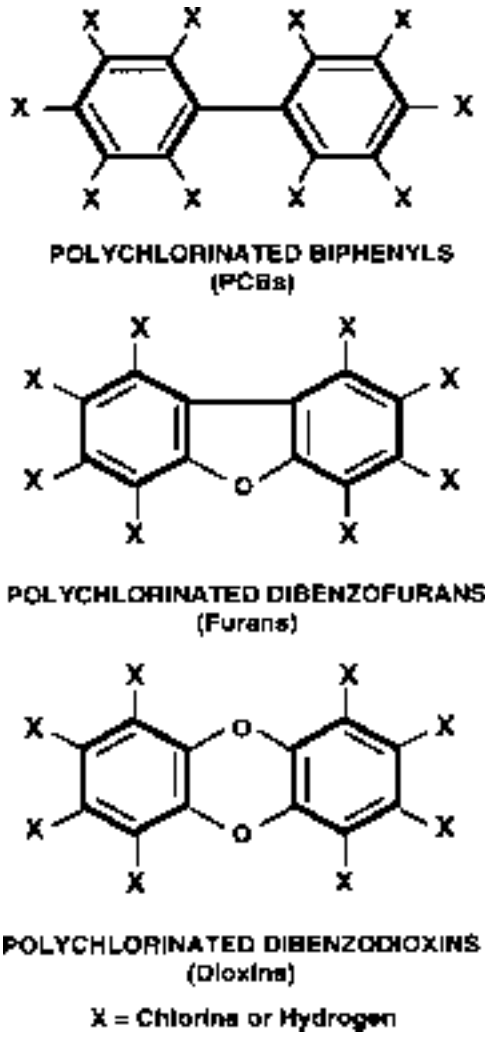


Figure 1. Polychlorinated Biphenyls and Related Compounds

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. Leaching of PCBs from soil is slow, particularly for the more highly chlorinated congeners,

- PCBs persist in the environment, concentrating upward in the food chain.

and translocation to plants via soil is insignificant. 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 (ATSDR 2000a). Inhalation of these volatilized compounds is one possible route of exposure in the general population, but it is not the primary route of exposure.

- The primary nonoccupational source of PCB exposure is food, especially fish from contaminated waters.

The primary route of exposure to PCBs in the general population appears to involve the consumption of contaminated foods, particularly meat, fish, and poultry (ATSDR 2000a). In aquatic environments, the high lipophilicity of PCBs causes these compounds to partition out of the water and become preferentially adsorbed to sediments. Although sediment adsorption is useful in preventing 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. As a result of this bioconcentration, PCB levels in aquatic organisms can be up to 1 million times higher than their concentration in the aquatic environment. 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 2000a).

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 that contains PCBs or as a result of accidents involving such equipment (ATSDR 2000a). 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 and televisions). The ballasts of older fluorescent light fixtures might also contain PCBs. During normal operation of these lights, the PCBs are entirely enclosed; when the capacitor wears out, however, it can burn or break and leak PCBs.

Occupational exposure to PCBs occurs mainly via the inhalation and dermal routes. Commercial PCB mixtures are colorless to dark brown oils, viscous liquids, or sticky resinous semisolids. Although they evaporate slowly at room temperature, the volatility of PCBs increases

dramatically with even a small increase in temperature. Overheated equipment that contains PCBs can vaporize significant quantities of these compounds, creating an inhalation hazard that can be magnified by poor ventilation. Because of their highly lipophilic nature, PCBs can also be absorbed through the skin following contact with contaminated equipment, water, or soil.

Challenge

In response to your persistent, detailed questioning about his work, hobbies and recreational activities, and possible contact with hepatotoxins, the patient reveals that while in the basement workshop he frequently wipes up a "dark, oily discharge" near a large electrical transformer that he collected in the work area. The discharge has also resulted in a gummy residue on tools and other surfaces. He mentions he sometimes feels dizzy and nauseated after working in the basement all day.

(1) Is there an association between the clinical findings and this additional information?

Who's At Risk

Consumption of contaminated sport fish, particularly bottom-feeding species from waters contaminated with PCBs, increases the level of exposure to PCBs. There is a direct relationship between serum PCB levels and the quantity of contaminated fish consumed. For example, serum PCB levels ranged from 7 parts per billion (ppb) in Michigan residents who ate no fish to a maximum of 366 ppb in persons who ate an average of 40 kg (88 pounds) of fish per year. There is also evidence to suggest that elevations in the serum PCB level are related to historic rather than recent levels of fish consumption (ATSDR 2000a).

- Recreational and subsistence fishers who eat large amounts of locally caught fish might be at increased risk for exposure to PCBs.

In addition to sport anglers and subsistence fishers (many of whom are American Indians, ethnic minorities, and immigrant populations), three other groups within the general population identified as having either a risk for elevated exposure or increased physiologic sensitivity to PCBs (ATSDR 2000a).

- Three other populations are also at risk for increased PCB exposure.

1. **The offspring of low income subsistence fishers mothers who ate large amounts of contaminated fish or wild game while pregnant.** Fetuses and neonates are potentially more sensitive to PCBs than are adults because the hepatic microsomal enzyme systems that facilitate the metabolism and excretion of PCBs are not fully functional. In addition, infants and young children consume a

greater amount of food per kilogram of body weight and therefore have a proportionately greater exposure to PCBs than do adults eating food with the same level of contamination (ATSDR 2000a). PCBs are lipophillic and there is placental transfer increasing the body burden.

2. **Farmers and their families who consume PCB-contaminated food via their own farm-raised beef and dairy cattle.** During the 1940s and 1950s, the inside of concrete silos on many farms in the Midwest 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 (ATSDR 2000a).

3. **People living near incinerators, other PCB-disposal facilities, or NPL hazardous waste sites where PCBs have been detected.** Persons living near incinerators, other PCB-disposal facilities, or any of the 432 current or former hazardous waste sites on the EPA NPL at which PCBs have been found are also at increased risk for exposure to PCBs (ATSDR 2000a).

- Persons with compromised hepatic function might metabolize PCBs less efficiently than healthy persons.

Because PCBs are metabolized mainly in the liver, persons with impaired hepatic function might be at increased risk because of their diminished ability to detoxify and excrete these compounds. Persons with incompletely developed glucuronide conjugation mechanisms (such as those with Gilbert syndrome or Crigler-Najjar syndrome) fall into this category, as do those with chronic liver diseases such as cirrhosis or hepatitis B. Because they temporarily decrease glucuronide synthesis, hepatic infections can increase a person's sensitivity to PCBs, as can the use of medications that are potentially toxic to the liver (ATSDR 2000a). Similarly, because hepatic function normally declines with age, elderly persons are also more susceptible to the effects of PCB exposure.

- Although PCBs are no longer manufactured in the United States, some workers can be exposed during repair of older equipment and accidents or spills.

Although PCBs are no longer manufactured in the United States, a potential for workplace exposure exists. Workers can inhale or have dermal contact with PCBs during the repair or routine maintenance of older equipment or electrical transformers and during accidents or spills involving PCBs. Exposure can also occur during the disposal of PCB-containing materials at hazardous waste sites. Occupations with risk for PCB exposure include, but are not limited to

- electric cable repair,
- electroplating,
- emergency response,

- firefighting,
- hazardous waste hauling/site operation,
- heat exchange equipment repair,
- maintenance cleaning,
- medical laboratory technician/technologist,
- metal finishing,
- noncellulose fiber industry,
- paving and roofing,
- pipefitting/plumbing,
- semiconductor and related industries,
- timber products manufacturing,
- transformer/capacitor repair, and
- waste oil processing.

Challenge

(2) Are other sources of PCB exposure likely for the patient described in the case study?

Biologic Fate

Although PCBs are readily absorbed into the body, they are only slowly metabolized and excreted. Animal studies suggest that absorbed PCBs partition between the aqueous and lipid compartments of the body in a biphasic pattern. After first distributing preferentially to the liver and muscle tissue, PCBs are subsequently redistributed to the adipose tissue, skin, and other fat-containing organs.

- PCBs are stored in adipose tissues.

The liver is the primary site of PCB metabolism, which occurs via hydroxylation and conjugation with glucuronic acid and sulfates. Glucuronide and sulfate conjugates are excreted mainly in the urine, whereas hydroxylated metabolites are excreted mainly in the bile.

- The liver is the primary site of PCB metabolism.

The rate of individual congener metabolism depends on the number and position of chlorine atoms. In rats, the half-lives of PCB congeners range from 1 to 460 days, depending on the degree of chlorination. In general, less-chlorinated isomers are more readily metabolized than are more highly chlorinated congeners. As a result of this preferential metabolism, more 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.

- The slow metabolism of PCBs leads to bioaccumulation.

Excretion of PCBs is very slow, so bioaccumulation occurs even at low exposure levels. As long as exposure continues, a true steady state is never achieved. Background levels of PCBs in human sera are typically <20 ppb and residues measured in human milk have values ranging from 40 to 100 ppb. Reported levels in adipose tissue range from 1 to 2 ppm.

Challenge

(3) Explain why patients with Gilbert syndrome might be at increased risk for adverse effects due to PCB exposure.

Physiologic Effects

- Adverse dermatologic, reproductive and developmental, endocrine, hepatic, and immunologic effects have been associated with exposure to PCBs.

Evidence on the physiologic effects of exposure to PCBs has been obtained from

- studies of industrial workers exposed to PCB-containing mixtures in the course of their work,
- two episodes of mass poisoning that occurred in Japan (the 1968 Yusho incident) and Taiwan (the 1979 Yu-Cheng incident), and
- studies of adults and children exposed to PCBs as a result of consuming contaminated sport fish.

In the two Asian episodes, exposure to PCBs occurred via the consumption of 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 about the extent to which the physiologic effects observed in the Yusho and Yu-Cheng populations can legitimately be attributed to PCBs, as opposed to the dibenzofuran co-contaminants.

Dermatologic Effects

- PCB-induced chloracne can be a sign of systemic toxicity.

Chloracne is the only overt effect of PCB exposure in humans. In a person with PCB-induced chloracne, the acneform 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 (ATSDR 2000a).

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 from 1 to 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.

Chloracne generally indicates systemic toxicity and can result not only from dermal contact but also from ingestion of PCBs. However, the absence of chloracne does not rule out exposure. 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 to decades.

In addition to chloracne, persons in the Yusho population had hyperpigmentation of the skin, conjunctivae, gingivae, and nails. These pigmentation disturbances have also been noted in some PCB-exposed workers.

Reproductive and Developmental Effects

Recent studies indicate that consumption of PCB-contaminated fish can cause disturbances in reproductive parameters and cause 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 (AAP 1999).

- Reproductive function can be disrupted by exposure to PCBs, although more research is required to assess this possibility.

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 (ATSDR and EPA 1998). Some of these effects have also been reported in human populations. In a study of 626 married couples in Michigan, the relative risk of conception failure (defined as an inability to conceive after 12 months) increased in men but not in women with increasing consumption of PCB-contaminated fish. Some evidence shows that menstrual cycle length can be reduced with increased PCB intake, 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 multigravada women, no significant association was found between low to moderate PCB intake and clinically recognized spontaneous fetal death (ATSDR and EPA 1998).

- Neurobehavioral and developmental deficits have been reported in newborns exposed to PCBs in utero, and these deficits continue in school-aged children.

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 (ATSDR and EPA 1998). 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 6 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 g), and head circumference (0.6 cm); neurobehavioral deficits included depressed responsiveness, impaired visual recognition, and poor short-term memory. In addition, the 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 than infants born to women who had consumed less fish (ATSDR and EPA 1998). **Women in their childbearing years must be aware of fish advisories.**

Follow-up studies of the children from this cohort have demonstrated that the effects of perinatal exposure to PCBs are persistent. At 4 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, were twice as likely to lag behind at least 2 years in reading comprehension, and were more likely to have difficulty paying attention (ATSDR and EPA 1998).

Similar developmental and neurobehavioral deficits have been reported in children born to women who were pregnant during the Yusho and Yu-Cheng incidents. Developmental delays were seen at all ages and were greater in children who were smaller in size, had neonatal signs of intoxication, and/or had a history of nail deformities. Follow-up testing indicated that effects on cognitive development persisted for several years after exposure (ATSDR and EPA 1998).

Endocrine Effects

- PCBs can mimic or disrupt the action of thyroid and/or female sex hormones.

PCBs have been identified as possible environmental endocrine modulators (chemicals that mimic or disrupt the action of naturally occurring hormones) (ATSDR 2000a). The best understood effects of PCB exposure on endocrine function involve disturbances in processes normally mediated by thyroid and female sex hormones.

The thyroid gland is an unequivocal target of PCBs in rats, and limited but corroborative occupational data indicate a potential for thyroidotoxic effects in humans (ATSDR 2000a). In a Dutch population, elevated PCB

levels correlated with lower maternal levels of circulating triiodothyronine and total thyroxine and with higher plasma levels of thyroid-stimulating hormone 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 (ATSDR and EPA 1998). In another study, hypotonia at birth was related to prenatal PCB exposure in infants who also exhibited elevated levels of thyrotropin (AAP 1999).

Because thyroid hormones are essential for normal behavioral, intellectual, and neurologic development, it is possible that the deficits in learning, memory, and attentional processes observed in the offspring of PCB-exposed women 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 (AAP 1999), suggesting a possible mechanism of thyroidotoxicity. Hydroxylated PCB metabolites appear to be particularly potent in this regard (ATSDR 2000a).

Other subsets of PCB congeners might interfere with the biological effects of estrogen. Depending on the spatial orientation of their chlorine constituents, some congeners exhibit weak estrogenic activity, whereas others act as antiestrogens (ATSDR 2000a). The implications of this activity for human health are not well understood. In the Taiwanese Yu-Cheng population, adolescent males who had been exposed to high PCB levels in utero progressed normally through the Tanner stages but had smaller penises than did controls (AAP 1999). Girls who were similarly exposed exhibited a growth delay but otherwise normal development at puberty. It is not known, however, whether either of these effects was estrogenic (AAP 1999).

Hepatic Effects

Histologically documented liver damage is a consistent and prominent finding among PCB-exposed animals; however, no evidence of hepatic dysfunction or overt hepatotoxicity has been seen in PCB-exposed workers (ATSDR 2000a). 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 (ATSDR and EPA 1998). Asymptomatic hepatomegaly has been reported in exposed workers, many of whom had concomitant elevated serum PCB levels.

- Although liver damage is common in PCB-exposed animals, overt hepatotoxicity is uncommon in humans.

Strong evidence shows that exposure to PCBs can increase serum liver enzyme levels. Some researchers believe that aspartate aminotransferase

- Exposure to PCBs can increase serum levels of hepatic enzymes and can induce microsomal enzyme function.

(SGOT or AST) and gamma glutamyl transpeptidase (GGTP or GGT) are the most sensitive indicators of PCB exposure in humans, and that changes in these enzymes can occur at exposure levels below those at which chloracne appears.

Increases in urinary porphyrin levels were noted in a study of workers with low-level PCB exposure, an effect that is believed to be secondary to the induction of hepatic microsomal enzymes. Total bilirubin levels exhibit a positive correlation, and serum albumin a negative correlation, with serum PCB levels (ATSDR and EPA 1998). The reported effects of PCB exposure on serum triglycerides and cholesterol have been inconsistent, and are probably related to the partitioning effects of PCBs. Those correlations that have been reported do not appear to be of toxicologic significance because they were observed in persons with normal lipid levels (ATSDR 2000a). In animal studies, reductions in the hepatic storage capacity for vitamin A have also been reported (ATSDR 2000a), but the implications of this finding for human health are not known.

Microsomal enzyme induction by PCBs has been observed in the liver of humans and in extrahepatic tissues of animals (ATSDR 2000a). Different PCB mixtures may induce a variety of the CYP (P450) family of enzymes. The set of enzymes induced depends on the particular PCBs in the mixture; sometimes the induced enzymes are similar to those induced by Phenobarbital, other times different distinctive sets of enzymes are induced, and sometimes there is no enzyme induction. Enzyme induction may affect how rapidly both endogenous (e.g. hormones) or exogenous substances (drugs, environmental metabolites, etc.) are metabolized.

Carcinogenicity

- On the basis of results from high-dose animal studies, PCBs are considered probable human carcinogens (Group 2A classification, International Agency for Research on Cancer).

The results of epidemiologic studies have raised concerns about the potential carcinogenicity of PCBs. In studies of occupationally exposed workers, increases in the incidence of malignant melanoma and cancers of the liver, gall bladder, biliary tract, and brain have been reported. In persons without known occupational exposure to PCBs, elevations in the serum PCB level have been associated with an increased risk of non-Hodgkin lymphoma (ATSDR and EPA 1998). Because of their estrogenic properties, PCBs have also been proposed as possible inducers of breast cancer; however, the results of epidemiologic studies in PCB-exposed women have been inconsistent (ATSDR 2000a).

At present, the weight of evidence from human studies does not support a causal association between PCBs and human cancer (ATSDR 2000a). Limitations in the design of these studies and the inconsistency of results

from one population to another make it difficult to ascertain whether the observed effects were causally related to PCB exposure. However, data from animal studies have clearly shown that PCBs cause hepatocarcinomas, pituitary tumors, leukemia, lymphomas, and gastrointestinal tract tumors. On the basis of these data, EPA considers PCBs a probable human carcinogen.

Other Effects

Occupational and epidemiologic studies have suggested or demonstrated other adverse health effects from exposure to PCBs, including effects involving the neurologic, cardiovascular, immune, musculoskeletal, and gastrointestinal systems.

- Additional adverse effects of PCBs involve the neurologic, cardiovascular, immune, musculoskeletal, and gastrointestinal systems.

In southwest Quebec, adults who ate fish from PCB-contaminated waters had significantly greater motor retardation, poorer results on certain tests of memory and attention, and higher scores on a standardized confusion scale than did controls, and these neurologic deficits were directly related to the frequency of fish consumption (ATSDR and EPA 1998).

In a study of persons living near a hazardous waste site, the incidence of borderline and definite hypertension was 30% greater among PCB-exposed persons than among controls, and the increases in blood pressure were significantly associated with serum PCB levels (ATSDR and EPA 1998). However, the existing data are insufficient to infer possible cardiovascular toxicity of PCBs in humans (ATSDR 2000a).

Immune system effects reported in PCB-exposed populations have included decreases in natural killer cell count, decreases in IgA and IgM antibody levels, alterations in the ratio of helper to killer (CD4+/CD8+) T-cells, and decreases in monocyte and granulocyte counts. 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 (ATSDR and EPA 1998).

Joint pain occurs in 11% of workers exposed to PCB-containing mixtures (ATSDR 2000a). This rate is similar to the 10% incidence of unspecified joint pain reported in farm families who consumed beef and dairy products contaminated with PCBs (ATSDR and EPA 1998). However, the cause of joint pain and its association with PCB exposure remain uncertain.

Appetite loss has been reported in transformer and electrical equipment manufacturing workers exposed to various PCB-containing mixtures

(ATSDR and EPA 1998). Other nonspecific gastrointestinal symptoms experienced by workers exposed to PCBs include nausea, epigastric distress and pain, and intolerance to fatty foods (ATSDR 2000a).

Challenge

(4) Is there a need to be concerned about PCB exposure when the clinical effects in this patient seem so limited?

Clinical Evaluation

History and Physical Examination

A detailed history will facilitate the diagnosis of chronic PCB poisoning. Pertinent information includes occupational histories of all household members as well as information on the patient's medications and diet, including ethanol intake and sport fish consumption. 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

- Chloracne is the only known overt sign of PCB toxicity; however, the absence of chloracne does not rule out exposure.

PCBs have very low potential for producing acute toxic effects. The only overt sign of PCB exposure is chloracne, which is described in the Dermatologic Effects section. Acneform 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.

Elevated liver enzymes are the most sensitive indicator of PCB exposure in animals, and alterations in AST (SGOT), GGT (GGTP), bilirubin, and albumin levels have been consistently reported in human epidemiologic studies. Hepatomegaly has also been noted in some PCB-exposed workers.

Chronic Exposure

- Signs of chronic exposure to PCBs are generally subtle, if present at all.

Many people who are chronically exposed to PCBs exhibit no overt signs or symptoms of toxicity. In persons with hepatic involvement, signs of PCB exposure can include weight loss, anorexia, nausea, vomiting, jaundice, and abdominal pain. Headache, dizziness, and edema have also been reported.

Laboratory Tests

Direct Biologic Indicators

Some researchers believe that PCB levels in the serum and adipose tissues provide a reliable measurement of long-term exposure. Although PCB levels in the serum and other tissues can be measured by many laboratories, there are no standardized techniques for quantifying these compounds, and no reference values against which patient samples can be compared. Because these tests are likely to be inconclusive as well as expensive and time-consuming, analysis of either serum or adipose tissue samples is not recommended unless the exposure has been massive. In all but the most extreme cases, therefore, the diagnostic workup should be limited to liver function tests and dermatologic examination, with skin biopsy of lesions.

- Serum or adipose tissue PCB levels can indicate exposure, but they are difficult to interpret clinically.

The question of measuring PCB levels most frequently arises in the context of discussions about breastfeeding. Although PCBs accumulate in breast milk, and breast-fed infants might be at additional risk because human milk contains a steroid that inhibits PCB metabolism and excretion (ATSDR 2000a), 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. In unusual circumstances, local health department officials who are aware of the PCB problems in the region where high exposures have occurred should be consulted (AAP 1999).

- The American Academy of Pediatrics (AAP) does not recommend testing breast milk for PCBs, and encourages breastfeeding in all but the most unusual circumstances.

Indirect Biologic Indicators

In the absence of chloracne, liver function tests provide the most consistent evidence of PCB toxicity; however, these tests are of questionable value because they are nonspecific. Also, normal liver enzyme values do not rule out significant exposure; body burden still might be elevated. PCB conjugates can often be detected in urine after exposure, but their analysis is expensive, unreliable, and not recommended.

- Elevated hepatic enzyme levels are of limited value in diagnosing exposure to PCBs.

Challenge

(5) What confirmatory laboratory test can be ordered to establish the diagnosis of PCB exposure?

(6) The patient requests a serum PCB analysis. The laboratory reports a level of 125 ppb, with no normal range indicated. How will you interpret this report?

Treatment and Management

Acute Exposure

- No antidote exists for PCB exposure; therefore, treatment is symptomatic.

In the event of PCB splashes in the eyes, irrigate with tepid water immediately for at least 15 minutes, and follow with ophthalmic evaluation. Remove contaminated clothing and discard properly. Gently wash affected skin with soap and warm water for at least 15 minutes.

In the rare event that PCB-containing substances are ingested, immediately induce vomiting if the patient is conscious. Gastric lavage can be subsequently administered at a medical facility until the gastric washings are clear. Activated charcoal has not been proven beneficial, but is not contraindicated. Exposed persons should have periodic follow-up examinations with particular attention to hepatic function and dermal lesions.

Chronic Exposure

- The goal of treatment in chronically exposed patients is to prevent any additional exposure to PCBs.

No specific treatment exists for chronic exposure to PCBs. Because no known methods exist for reducing the reserves of PCBs in adipose tissues, attempts to purge the body of PCBs should not be made. Cholestyramine therapy, sauna bathing, and fasting have all been attempted and have proven unsuccessful (AAP 1999). In fact, PCBs stored in fat can be mobilized by the patient's crash dieting.

Initial treatment of chloracne is based on cessation of exposure, good skin hygiene, and dermatologic measures commonly used for acne vulgaris. If these measures are not effective, the patient should be referred to a dermatologist.

If chronic exposure has occurred as a result of consuming contaminated fish or game, the patient should be informed of the tendency for PCBs 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 specifying the bodies of water or hunting areas where fish and game are likely to be contaminated with PCBs and listing 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 consumed. To minimize the risk for further exposure among sport and subsistence fishers, these persons should be encouraged to familiarize themselves with and observe advisory recommendations (ATSDR 2000a).

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 offspring of mothers who ate large amounts of contaminated fish or wild game while pregnant. Fetuses and neonates are potentially more sensitive to PCBs than are adults because the hepatic microsomal enzyme systems that facilitate the metabolism and excretion of PCBs are not fully functional. In addition, infants and young children consume a greater amount of food per kilogram of body weight and therefore have a proportionately greater exposure to PCBs than do adults eating food with the same level of contamination (ATSDR 2000a).

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 1999).

Challenge

(7) What steps should be recommended to patients when PCB-related health effects are suspected?

Standards and Regulations

Workplace

Air

The Occupational Safety and Health Administration's (OSHA) permissible exposure limit (PEL) is a time-weighted average (TWA) airborne concentration of 1,000 micrograms per cubic meter ($\mu g/m^3$) for PCBs containing 42% chlorine (average molecular formula of $C_{12}H_7Cl_3$). The PEL for PCBs with 54% chlorine and an average molecular formula of $C_{12}H_5Cl_5$ is 500 $\mu g/m^3$. Both standards encompass all physical forms of these compounds: aerosols, vapor, mist, sprays, and PCB-laden dust particles. OSHA recognizes that PCBs are absorbed through intact skin; therefore, both dermal and inhalation exposure routes should be evaluated by an industrial hygienist.

- OSHA's PEL is 1,000 $\mu g/m^3$ for PCBs containing 42% chlorine and 500 $\mu g/m^3$ for compounds containing 54% chlorine.

The National Institute for Occupational Safety and Health (NIOSH) recommends a 10-hour TWA of 1 $\mu g/m^3$ based on the minimum reliable detectable concentration and the potential carcinogenicity of PCBs. NIOSH also recommends that all workplace exposures be reduced to the lowest feasible level.

Environment

Water

- EPA's enforceable maximum contaminant level for PCBs in public drinking water systems is 0.0005 ppm.

EPA considers PCBs a probable human carcinogen and prohibits industrial discharges under the Clean Water Act Effluent Guidelines. The EPA drinking water maximum contaminant level goal is zero and the enforceable maximum contaminant level for PCBs in public water systems is 0.0005 ppm (EPA 2001). EPA also requires that spills or accidental releases into the environment of 1 pound or more of PCBs be reported to EPA (ATSDR 2000a).

Food

- The Food and Drug Administration (FDA) tolerance levels for PCBs in food range between 0.2 and 3 ppm.

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

The allowable daily intake set for PCBs by the Food and Agriculture Organization and the World Health Organization is 6 ìg/kg per day (AAP 1999).

Challenge

(8) What additional steps should be taken for the situation described in the case study?

Suggested Reading List

*References cited in text.

Clinical

[AAP] American Academy of Pediatrics. 1994. Policy statement: PCBs in breast milk. Pediatrics 94:122–3.

*[AAP] American Academy of Pediatrics. 1999. Polychlorinated biphenyls, dibenzofurans, and dibenzodioxins. In: Etzel RA, Balk SJ, editors. Handbook of Pediatric Environmental Health. p. 215–22.

Chai S, Bearer CF. 1999. A developmental approach to pediatric environmental health. Washington (DC): Children's Environmental Health Network; 1999.

Jacobson L, Jacobson SW. 1996. Intellectual impairment in children exposed to polychlorinated biphenyls in utero. N Engl J Med 335:783–9.

Kimbrough RD. 1987. Human health effects of polychlorinated biphenyls (PCBs) and polybrominated biphenyls (PBBs). Annu Rev Pharmacol Toxicol 27:87.

Letz G. 1983. The toxicology of PCBs: an overview for clinicians. West J Med 534–40.

McKenna JP, Moskovitz M, Cox JL. 1989. Abnormal liver function tests in asymptomatic patients. Am Fam Physician 39(3):117–26.

Nicholson WJ, Landrigan PJ. 1994. Human health effects of polychlorinated biphenyls. In: Schecter A, editor. Dioxins and health. New York: Plenum. p. 487–524.

Epidemiology

Acquavella JF, Hanis NM, Nicolich MJ, Phillips SC. 1986. Assessment of clinical, metabolic, dietary, and occupational correlations with serum polychlorinated biphenyl levels among employees at an electrical capacitor manufacturing plant. J Occup Med 28(11):1177–80.

Fein GG, Jacobson JL, Jacobson SW, Schwartz PM, Dowler JK. 1984. Prenatal exposure to polychlorinated biphenyls: effects on birth size and gestational age. J Pediatr 105:315–20.

Fischbein A, Wolff MS, Bernstein J, Selikoff IJ. 1982. Dermatological findings in capacitor manufacturing workers exposed to dielectric fluids containing polychlorinated biphenyls (PCBs). Arch Environ Health 37(2):69–74.

Weaver G. 1983. PCB contamination in and around New Bedford, Mass. Environ Sci Technol 18:22A–7A.

Toxicology

Cogliano VJ. 1998. Assessing the cancer risk from environmental PCBs. Environ Health Perspect 106:317–23.

Fischbein L. 1974. Toxicology of chlorinated biphenyls. Annu Rev Pharmacol 14:139–56.

[IARC] International Agency for Research on Cancer. 1987. IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans. Suppl 7. Update of IARC monographs volumes 1–42. Lyon, France: International Agency for Research on Cancer.

Related Documents

*[ATSDR] Agency for Toxic Substances and Disease Registry. 2000a. Toxicological profile for polychlorinated biphenyls (update). Atlanta: US Department of Health and Human Services.

[ATSDR] Agency for Toxic Substances and Disease Registry. 2000b. ToxFAQs. Available from URL: www.atsdr.cdc.gov/toxfaq.html.

*[ATSDR] Agency for Toxic Substances and Disease Registry and [EPA] US Environmental Protection Agency. 1998. Public health implications of exposure to polychlorinated biphenyls (PCBs). Atlanta: US Department of Health and Human Services.

*[EPA] US Environmental Protection Agency. 1992a. National Study of Chemical Residues in Fish, volume 1. Washington (DC): US Environmental Protection Agency. EPA Report No.: EPA 823-R-92-008a.

*[EPA] US Environmental Protection Agency. 1992b. National Study of Chemical Residues in Fish, volume 2. Washington (DC): US Environmental Protection Agency. EPA Report No.: EPA 823-R-92-008b.

[EPA] US Environmental Protection Agency. 1995. Report to Congress: the effects of Great Lakes contaminants on human health. Washington (DC): US Environmental Protection Agency. EPA Report No. 905-R-95-017.

[EPA] US Environmental Protection Agency. 1998. Drinking water criteria document for polychlorinated biphenyls (PCBs). Washington (DC): US Environmental Protection Agency. EPA Report No. ECAO-CIN-414.

*[EPA] US Environmental Protection Agency, Office of Ground Water and Drinking Water. 2001. Current drinking water standards. Washington (DC): US Environmental Protection Agency. Available from URL: www.epa.gov/safewater/mcl.html.

*[EPA] US Environmental Protection Agency. 2002. A guide to healthy eating of the fish you catch. Washington (DC): US Environmental Protection Agency. EPA Report No. 823-F-02-005. Available from URL: www.epa.gov/waterscience/fish/30cwafish.pdf.

[NIOSH] National Institute for Occupational Safety and Health. 1999. NIOSH pocket guide to chemical hazards. Cincinnati (OH): National Institute for Occupational Safety and Health. Available from URL: www.cdc.gov/niosh/npg/pgdstart.html.

Answers to Pretest and Challenge Questions

Pretest

(a) 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 are clinically unexpected. Gilbert syndrome is a hereditary, relatively common, benign, unconjugated hyperbilirubinemia. It might contribute to the laboratory findings of elevated bilirubin (especially after a fast), but would not explain the clinical picture or elevated liver enzymes.

(b) The combination of asymptomatic hepatomegaly and mild nonspecific elevations of hepatic enzymes is suggestive of a chronic inflammatory liver process or hepatitis. The causes of hepatitis can be classified as drug-induced, toxic, infectious, genetic, and connective tissue disease-associated. The major cause of liver disease in the United States is ethanol ingestion. Less common are environmental exposures, resulting in either acute or chronic toxic hepatitis. Infectious hepatitis includes those due to the viruses such as A (infectious), B (serum), C (transfusion-associated), and other possible agents of non-A, non-B hepatitis. Some connective tissue diseases such as lupus erythematosus are associated with a specific type of 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 must be excluded.

(c) Viral serology and a heterophil antibody test should be considered. If suggestive signs or symptoms exist, a serum iron and total iron binding capacity, serum copper and ceruloplasmin, and antinuclear antibodies might be helpful. Assays for suspected hepatotoxins might also be of value. Further evaluation might include ultrasound and percutaneous liver biopsy if other tests do not provide sufficient information.

Challenge

(1) 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.

(2) In addition to the patient's possible exposure through dermal and inhalation contact, he might also be exposed through consumption of contaminated fish. Great Lakes fish, particularly from Lake Michigan, are a potential source of PCBs.

(3) Persons with Gilbert syndrome have decreased UDP-glucuronyltransferase activity, resulting in impaired glucuronidation of bilirubin and, presumably, of PCBs as well. Because one elimination pathway for PCBs is excretion of the glucuronide in urine, impaired capacity to conjugate PCBs with glucuronic acid could theoretically lead to accumulated PCBs and greater body burden. This hypothesis has not been tested, however.

(4) Yes. It is important to be aware that potential carcinogenicity is the main reason PCB production was banned in the United States. Human evidence is still considered inadequate, but the animal evidence is strong enough for EPA, NIOSH, and the International Agency for Research on Cancer (IARC) to conclude that PCBs are probably carcinogenic in humans (Group 2A classification).

(5) Testing human tissue for PCB content, therefore, remains principally a research tool.

Selected 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, can also be done. However, such tests are expensive and health risks often cannot be determined from the results.

(6) A correlation between increasing levels of serum PCBs and dermatologic findings, including chloracne, has not been consistently found in human epidemiologic studies. However, one study involving 153 workers with occupational exposure to PCBs showed 22 subjects with dermal abnormalities and a mean plasma PCB level of 87 ppb, whereas 131 subjects without abnormalities had a mean serum level of 50 ppb. The difference was statistically significant. By comparison, plasma PCB levels in unexposed populations are <30 ppb. However, no serum PCB values are yet accepted as normal or toxic levels. The case study patient's PCB serum level of 125 ppb is nonetheless consistent with PCB exposure as an etiology for his unusual acne, and PCB exposure might be contributing to the hepatic effects noted.

(7) 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 cleaned by a professional familiar with PCB removal. He should also refrain from eating fish from the Great Lakes until his PCB level normalizes and the

fish are known to be uncontaminated. Guidance is available on how to choose safer fish to eat and on safer ways to prepare and cook fish (EPA 2002). 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. No data exist to support monitoring serum PCB levels.

(8) Because cessation of exposure is of prime importance, the physician can be most helpful by specifically recommending proper abatement. 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 work cooperatively with those involved to bring about remediation of the harmful exposure. It is important to prevent others from using the basement areas until cleanup is complete. In addition, the patient should be informed of the availability of fishing and game advisories and should be encouraged to observe the recommendations of these advisories.

Other Sources of Information

More information on the adverse effects of PCBs and the treatment and management of PCB-exposed persons can be obtained from ATSDR, your state and local health departments, and university medical centers. For clinical inquiries, contact the Association of Occupational and Environmental Clinics (AOEC), the Pediatric Environmental Health Specialty Units (PEHSUs), ACMT, or the American Association of Poison Control Centers.

AOEC

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.

The primary goal of AOEC is to facilitate the prevention and treatment of occupational and environmental illnesses and injuries through collaborative reporting and investigation of health problems. AOEC members develop curriculum materials in occupational and environmental health and provide Education Activities (EA) programs for primary care practitioners and others.

For more information and a listing of AOEC clinics in your area, contact the AOEC office:

1010 Vermont Avenue, NW #513
Washington, DC 20005
Telephone: 202-347-4976
Fax: 202-347-4950
Web site: www.aoec.org.

PEHSUs

The PEHSUs are a resource for pediatricians, other health care providers, parents, teachers, the general public, and EPA and ATSDR staff members nationwide. PEHSUs provide medical education and training, consultation, and clinical specialty referrals. Health care providers can use this resource when responding to suspected clinical presentations, known exposures, and in community settings.

Ten PESHUs are now in operation across the United States; contact information for each unit is listed below. Check AOEC's Web site (www.aoec.org/pesu.htm) for the most up-to-date information on the units.

Region 1, Massachusetts:
Pediatric Environmental Health Center, Children Hospital, Boston
Telephone: 1-888-Child14
Web site: www.childrenshospital.org (In the "find" box, enter the key word "environmental")

Region 2, New York:
Mt. Sinai Pediatric Environmental Health Unit/Mt. Sinai-Irving J. Selikoff Center for Occupational and Environmental Medicine, New York
Telephone: 212-241-6173
Web site: www.mssm.edu/cpm/peds_environ.shtml

Region 3, Washington, District of Columbia:
Mid-Atlantic Center for Children's Health and the Environment (MACCHE), George Washington University, Washington, District of Columbia
Telephone: 1-866-MACCHE1 (1-866-622-2431)
Web site: www.health-e-kids.org

Region 4, Georgia:
The Southeast Pediatric Environmental Health Specialty Unit at Emory University, Atlanta
Telephone: 1-877-337-3478 (1-877-33PEHSU)
Web site: www.sph.emory.edu/PEHSU

Region 5, Illinois:
Great Lakes Center for Children's Environmental Health, Cook County Hospital, Chicago
Telephone: 1-800-672-3113 (toll-free) or 312-633-5310
Web site: www.uic.edu/sph/glakes/kids

Region 6, Texas:
Southwest Center for Pediatric Environmental Health, University of Texas Health Center at Tyler, Tyler, Texas
Telephone: 1-888-901-5665 (toll-free)
Web site: research.uthct.edu/swcpeh/

Region 7, Iowa:
Midwest Regional Pediatric Environmental Health Center, University of Iowa, Iowa City, Iowa
Telephone: 1-866-697-7342
Web site: www.uihealthcare.com/depts/pediatricenvironmentalhealth/index.html

Region 8, Colorado:
Rocky Mountain Regional Pediatric Environmental Health Specialty Unit, National Jewish Medical and Research Center, Denver
Telephone: 1-877-800-5554 (toll-free)
Web site: rmrpehsu.org

Region 9, California:

University of California-San Francisco (UCSF)/University of California-Irvine (UCI)
Pediatric Environmental Health Specialty Unit
Telephone: 1-415-206-4320 (for both sites)
Web site: www.ucsf.edu/ucpehsu

Region 10, Washington State:

Pediatric Environmental Health Specialty Unit, Harborview Medical Center, Seattle
Telephone: 1-887-KID-CHEM (toll-free west of the Mississippi River) or 206-526-2121
Web site: www.depts.washington.edu/oemp/grants/PEHSU.html

American College of Medical Toxicology (ACMT)

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, including scientific meetings, communication and networking, public policy, medical toxicology practice, and fellowship training in medical toxicology.

For more information about ACMT, contact the ACMT office:

American College of Medical Toxicology
777 East Park Drive
PO Box 8820
Harrisburg, PA 17105-8820
Web site: www.acmt.net
E-mail: ACMT@pamedsoc.org.

American Association of Poison Control Centers

Poison control centers were established in 1953 to help physicians and other clinicians deal with poisonings of adults and children in the United States. In 1983, the American Association of Poison Control Centers was established as the professional organization for poison control centers. The regional poison control centers can act as valuable resources in providing information about the toxicity and health effects of hazardous exposures involved in poisonings.

The local poison control center can specify the ingredients of common household products when labels do not provide adequate information.

Each certified poison control center is required to publicize its location and methods of contact. Typically, the contact telephone number can be found on the inside front cover of telephone books, where other emergency numbers are usually located.

The main emergency number across the country is 1-800-222-1222, although some states have other contact numbers as well as a number for the hearing impaired. For more information, contact the American Association of Poison Control Centers:

American Association of Poison Control Centers
3201 New Mexico Avenue, Suite 310
Washington, DC 20016
Telephone: (202) 362-7217
Web site: www.aapcc.org
E-mail: aapcc@poison.org.

For poisoning emergencies, call 1-800-222-1222. APCC does not manage poison exposure cases.

Notes

Case Studies in Environmental Medicine:

PCB Toxicity

Evaluation Questionnaire and Posttest, Course Number SS3067

Course Goal: To increase the primary care provider's knowledge of hazardous substances in the environment and to aid in the evaluation of potentially exposed patients.

Objectives

- Discuss the major route of exposure for PCBs.
- Describe two potential environmental and occupational sources of PCB exposure.
- Give two reasons why PCBs are a health hazard.
- Describe three factors contributing to PCB toxicity.
- Identify evaluation and treatment protocols for persons exposed to PCBs.
- List two sources of information on PCBs.

Tell Us About Yourself

Please carefully read the questions. Provide answers on the answer sheet (page 37). Your credit will be awarded based on the type of credit you select.

1. What type of continuing education credit do you wish to receive?
****Nurses should request CNE, not CEU. See note on page 36.**
A. CME (for physicians)
B. CME (for non-attending)
C. CNE (continuing nursing education)
D. CEU (continuing education units)
E. [Not used]
F. [Not used]
G. [Not used]
H. None of the above

2. Are you a...
A. Nurse
B. Pharmacist
C. Physician
D. Veterinarian
E. None of the above

3. What is your highest level of education?
A. High school or equivalent
B. Associate, 2-year degree
C. Bachelor's degree
D. Master's degree
E. Doctorate
F. Other

4. Each year, approximately how many patients with PCB exposure do you see?

A. None
B. 1–5
C. 6–10
D. 11–15
E. More than 15

5. Which of the following best describes your current occupation?

A. Environmental Health Professional
B. Epidemiologist
C. Health Educator
D. Laboratorian
E. Physician Assistant
F. Industrial Hygienist
G. Sanitarian
H. Toxicologist
I. Other patient care provider
J. Student
K. None of the above

6. Which of the following best describes your current work setting?

A. Academic (public and private)
B. Private health care organization
C. Public health organization
D. Environmental health organization
E. Non-profit organization
F. Other work setting

7. Which of the following best describes the organization in which you work?

A. Federal government
B. State government
C. County government
D. Local government
E. Non-governmental agency
F. Other type of organization

Tell Us About the Course

8. How did you obtain this course?

A. Downloaded or printed from Web site
B. Shared materials with colleague(s)
C. By mail from ATSDR
D. Not applicable

9. How did you first learn about this course?

A. State publication (or other state-sponsored communication)
B. *MMWR*
C. ATSDR Internet site or homepage
D. PHTN source (PHTN Web site, e-mail announcement)
E. Colleague
F. Other

10. What was the most important factor in your decision to obtain this course?

A. Content
B. Continuing education credit
C. Supervisor recommended
D. Previous participation in ATSDR training
E. Previous participation in CDC and PHTN training
F. Ability to take the course at my convenience
G. Other

11. How much time did you spend completing the course, evaluation, and posttest?

A. 1 to 1.5 hours
B. More than 1.5 hours but less than 2 hours
C. 2 to 2.5 hours
D. More than 2.5 hours but less than 3 hours
E. 3 hours or more

12. Please rate your level of knowledge before completing this course.

A. Great deal of knowledge about the content
B. Fair amount of knowledge about the content
C. Limited knowledge about the content
D. No prior knowledge about the content
E. No opinion

13. Please estimate your knowledge gain after completing this course.

A. Gained a great deal of knowledge about the content
B. Gained a fair amount of knowledge about the content
C. Gained a limited amount of knowledge about the content
D. Did not gain any knowledge about the content
E. No opinion

Please use the scale below to rate your level of agreement with the following statements (questions 14–25) about this course.

A. Agree
B. No opinion
C. Disagree
D. Not applicable

14. The objectives are relevant to the goal.

15. The tables and figures are an effective learning resource.

16. The content in this course was appropriate for my training needs.

17. Participation in this course enhanced my professional effectiveness.

18. I will recommend this course to my colleagues.

19. Overall, this course enhanced my ability to understand the content.

20. I am confident I can discuss the major route of exposure for PCBs.

21. I am confident I can describe two potential environmental and occupational sources of PCB exposure.

22. I am confident I can give two reasons why PCBs are a health hazard.

23. I am confident I can describe three factors contributing to PCB toxicity.

24. I am confident I can identify evaluation and treatment protocols for persons exposed to PCBs.

25. I am confident I can list two sources of information on PCBs.

Posttest

If you wish to receive continuing education credit for this program, you must complete this posttest. Each question below contains five suggested answers, of which one or more is correct. **Circle all correct answers on the answer sheet.**

26. Significant PCB exposure might occur as a result of

A. eating fish from PCB-contaminated waters.
B. exposure to leaking transformers.
C. eating a vegetarian diet.
D. inhaling soot or smoke from transformer or capacitor fires.
E. drinking ethanol beverages.

27. Although little is currently understood about the biologic fate of PCBs in humans, which of the following is (are) believed to be true?

A. PCB excretion is slow.
B. PCBs can bioaccumulate in adipose tissue.
C. Highly chlorinated congeners are more likely to be stored in the body than are less highly chlorinated PCBs.
D. The primary site of PCB metabolism is the liver.
E. PCB levels in serum are generally higher than those in adipose tissue or breast milk.

28. Populations that are believed to be at particular risk from PCBs include

A. recreational and subsistence fishers.
B. pregnant women and their offspring.
C. elderly people.
D. people of Spanish or Latino ancestry.
E. people living near incinerators.

29. PCB-induced chloracne is characterized by

A. diminished responsiveness to usual treatments for acne vulgaris.
B. lesions that average >20 mm in diameter.
C. cystic papules and comedones.
D. small grouped vesicles with regional lymph nodes enlarged.
E. a distribution that may include the periorbital area, chest, and buttocks.

30. Additional signs of PCB toxicity might include

A. weight loss.
B. ascites.
C. hepatomegaly.
D. abnormal liver function.
E. pancreatitis.

31. Which of the following statements is (are) false?

A. Chloracne can reflect systemic toxicity.
B. Liver enzymes are always elevated by PCBs.
C. Exposed populations have shown adverse developmental effects from PCBs.
D. PCBs are classified by the EPA as probable human carcinogens.
E. A sensitive indicator of PCB exposure in humans is cardiac dysfunction.

32. PCBs have been considered carcinogenic because

A. they are associated with increased rates of uterine cancer in humans.
B. they are immunosuppressive in humans.
C. they are associated with thymic atrophy in humans.
D. they are associated with increased rates of many cancers in animals.
E. evidence of their cancer-causing effects in humans is unequivocal.

33. In the treatment and management of PCB-exposed persons, you should

A. advise the patient to avoid further contact with potential sources of exposure.
B. caution against the use of other potentially hepatotoxic substances.
C. follow up with particular attention to hepatic function and dermal lesions.
D. initially treat chloracne the same as you would acne vulgaris.
E. place the patient on a crash diet to purge the body of PCBs.

Note to Nurses

CDC is accredited by the American Nurses Credentialing Center's (ANCC) Commission on Accreditation. ANCC credit is accepted by most State Boards of Nursing.

California nurses should write in "ANCC - Self-Study" for this course when applying for relicensure. A provider number is not needed.

Iowa nurses must be granted special approval from the Iowa Board of Nursing. Call 515-281-4823 or e-mail marmago@bon.state.ia.us to obtain the necessary application.

Case Studies in Environmental Medicine:

PCB Toxicity

Answer Sheet, Course Number SS3067

Instructions for submitting hard-copy answer sheet: Circle your answers. To receive your certificate, you must answer **all** questions. Mail or fax your completed answer sheet to

Fax: 770-488-4178, ATTN: Continuing Education Coordinator

Mail: Continuing Education Coordinator
Agency for Toxic Substances and Disease Registry
Division of Toxicology and Environmental Medicine
1600 Clifton Road, NE (MS F-32)
Atlanta, GA 30333

Be sure to fill in your name and address on the back of this form.

Remember, you can access the case studies online at www.atsdr.cdc.gov/HEC/CSEM/ and complete the evaluation questionnaire and posttest online at www2.cdc.gov/atsdrce/.

Online access allows you to receive your certificate as soon as you complete the posttest.

1. A B C D E F G H
2. A B C D E
3. A B C D E F G
4. A B C D E
5. A B C D E F G H I J K
6. A B C D E F
7. A B C D E F
8. A B C D
9. A B C D E F
10. A B C D E F G
11. A B C D E
12. A B C D E
13. A B C D E
14. A B C D
15. A B C D
16. A B C D
17. A B C D
18. A B C D
19. A B C D
20. A B C D
21. A B C D
22. A B C D
23. A B C D
24. A B C D
25. A B C D
26. A B C D E
27. A B C D E
28. A B C D E
29. A B C D E
30. A B C D E
31. A B C D E
32. A B C D E
33. A B C D E

Name: E-mail (not required):

Address:

Zip code:

○ Check here to be placed on the list to pilot test new case studies

fold here first

Place Stamp Here

Continuing Education Coordinator

Agency for Toxic Substances and Disease Registry

Division of Toxicology and Environmental Medicine

1600 Clifton Road, NE (MS F-32)

Atlanta, GA 30333

fold here second

Access the case studies online at www.atsdr.cdc.gov/HEC/CSEM/ and complete the evaluation questionnaire and posttest online at www2.cdc.gov/atsdrce/.

Online access allows you to receive your certificate as soon as you complete the posttest.

tape or staple here

**DEPARTMENT OF HEALTH
AND HUMAN SERVICES**
Agency for Toxic Substances
and Disease Registry
Division of Toxicology and
Environmental Medicine (MS F-32)
Atlanta, GA 30333
