Clinician Overview: Polychlorinated Biphenyls Transcript

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The goals for this presentation include increasing the ability of primary care clinicians to address potential health impacts associated with polychlorinated biphenyls or PCBs, providing guidance for the clinical evaluation and management of patients exposed to PCBs, and discussing prevention strategies and risk reduction.

At the end of the presentation, participants should be able to list properties and sources of PCBs, describe routes of exposure, explain potential health effects, describe the appropriate evaluation and management following exposure, describe patient follow-up recommendations, and describe risk and exposure reduction strategies.

To begin, we will discuss the properties of PCBs.

Polychlorinated biphenyls, also known as PCBs, are a family of manufactured chemicals that consist of a pair of connected benzene rings with one or more attached chlorine atoms. Depending on the number and position of chlorine atoms, two hundred nine different PCB substances, or congeners, may be formed. Different congeners may have varying chemical and toxic properties.

PCBs were previously widely used in multiple industrial and commercial applications due to their insulating properties. Production was banned in the US in 1979, when their health effects and ability to accumulate in the environment became known.

Commercial PCB products consisted of complex mixtures containing many different congeners. Therefore, people are typically exposed to many different congeners rather

than a single substance. PCB mixtures were often contaminated with other chemicals such as dioxins and dibenzofurans. Sometimes these contaminants may be more toxic than PCBs themselves. This makes it challenging to study the health effects associated with PCB exposure.

Group I PCBs are metabolized by hydroxylation and have estrogenic effects. They have half-lives of several months.

Group II PCBs interact with the aryl hydrocarbon receptor, causing induction of certain cytochrome P450 enzymes such as CYP1A and CYP2A1. They have properties similar to dioxins, including antiestrogenic activity and affecting the metabolism of carcinogens and estradiol. Their half-lives are 1 to 5 years.

Group III PCBs primarily induce the cytochrome P450 enzyme CYP2B, but also have some CYP1A1 and CYP2A1 activity. They have weak estrogenic activity and may affect the metabolism of estrogen and certain carcinogens. Their half-lives can be greater than ten years.

Next, we will discuss sources of PCBs.
PCBs were formerly used in multiple industrial applications, and structures built or renovated between 1950 and 1979 may contain them.

They may be found in old electrical equipment such as transformers and capacitors, heat exchange and dielectric fluids, and fluorescent light ballasts.

Many construction materials such as paint, adhesives, caulk, and ceiling tiles also contained them.

Consumer products such as inks and carbonless transfer paper are additional sources.

Other materials that contain PCBs include various fluid and oils used for lubrication, hydraulics, diffusion pumps, plasticizers, flame retardants, and pesticide extenders.

Even though PCBs are no longer commercially produced in the US, they are resistant to biodegradation. They can persist in the environment for months to years. They are highly lipophilic, which allows them to adsorb to soil and sediment and be readily absorbed by aquatic life.

In aquatic ecosystems, they can biomagnify upward through the food chain, becoming more concentrated in the tissues of larger animals. Cycling within the ecosystem may also occur, starting when PCBs are volatilized from land and water surfaces into the atmosphere. They can then deposit by rain, snow, particulates, or gases.

Now that we have discussed where PCBs are found, we are going to talk about how people may be exposed to them.

Exposure can happen via ingestion, inhalation, and dermal absorption.
The main route of PCB exposure for the general population is through consumption of contaminated foods. Levels may be higher in certain fish, meat, dairy, and poultry foods although concentrations in the food supply have decreased over time.

Fish from contaminated waters may contain high levels of PCBs from the environment. People who fish for sport or subsistence may eat contaminated fish frequently. Many of these people at risk are recreational fishers, Native Americans, ethnic minorities, immigrants, and other groups who rely on fishing as a food source.

Children of mothers who ate contaminated fish or wild game frequently while pregnant may have higher exposures as well.

In the 1940s and 1950s, many farms in the midwestern US had concrete silos coated with PCB containing sealants. These materials peeled off over time and became mixed with silage used to feed beef and dairy cattle. Farming families with these old silos who consume food produced from their own livestock may have been exposed to PCBs.

Children may be especially susceptible to PCB exposure, as they play on the floor and often put their hands inside their mouths. Additionally, dust and other PCB containing residues from paints, caulk, and other materials in old buildings can be ingested.

Children also consume a greater amount of food per kilogram of body weight compared to adults. Therefore, they may have proportionally greater exposure compared to adults when eating food with the same level of PCB contamination.

PCBs readily cross the placenta during pregnancy and accumulate in breast milk. In-utero and breastfeeding exposure may occur in children of exposed mothers who frequently eat contaminated fish. Fetuses and neonates are potentially more sensitive to exposure than adults because their immature enzyme systems may not metabolize and excrete PCBs efficiently and because of their rapidly developing tissues, organs, and systems.

However, given the scientific understanding at this time, the benefits of breastfeeding outweigh any potential risks of PCB exposure through breast milk. With numerous protective health benefits, breast milk continues to be the ideal nutrition for infants. In nearly every circumstance, the Centers for Disease Control and Prevention and the American Academy of Pediatrics recommend that nursing mothers continue to breastfeed their babies despite the potential presence of environmental contaminants.

People may also inhale PCBs. Inhalational exposures are primarily occupational. Although PCBs evaporate slowly at room temperature, their volatility increases when heated. For example, overheating of old electrical equipment may result in significant inhalational exposure. Buildings constructed or renovated between 1950 and 1979 may contain PCBs in caulk, paints, adhesives, fireproofing materials, ceiling tiles, and fluorescent light ballasts, which may lead to inhalation of PCB contaminated dust.

Children may be more likely to inhale PCB contaminated dust, given their shorter stature and tendency to play on the ground. They also have a higher minute ventilation than adults, meaning that they inhale and exhale a larger amount of air for their size compared to adults.

Finally, PCBs are highly lipophilic so can be absorbed through the skin with direct contact. Most of these exposures are occupational.

Next, we will highlight populations at risk for exposure to PCBs.
Workers in certain occupations may be at higher risk for exposure.
People who repair and work with electrical equipment may come into contact with old components that contain PCBs.

Workers in hazardous waste sites and waste oil processing facilities may be exposed as well.

Occupational exposure may occur among people who work in semiconductor manufacturing, metal finishing and electroplating, manufacturing of timber products, plumbing, paving and roofing, firefighting, and certain medical laboratories.

People may be exposed from the surrounding environment in areas where there are toxic waste sites, municipal landfills, Superfund sites, and where illegal or improper waste dumping may have occurred.

People who spend long periods of time in buildings containing old construction materials may also be at higher risk of exposure. These include children who attend school in buildings constructed or renovated between 1950 and 1980.

Now we will discuss the potential health effects of PCB exposure.
An exposed individual's risk depends on many factors. These include the exposure dose, exposure concentration, timing, frequency, and duration. A person's genetic and behavioral characteristics may also affect their risk.

Most environmental exposures are difficult to quantify in terms of dose, concentration, frequency, and duration. People are typically exposed to complex mixtures that contain many different congeners. These mixtures may be contaminated with other substances such as dioxins and dibenzofurans, which may be even more toxic than the PCBs.

One example of a mass poisoning event involving PCBs was the Yusho incident. In Japan in 1978, PCBs, polychlorinated dibenzofurans or PCDFs, and polychlorinated dibenzo-p-dioxins or PCDDs leaked into rice bran oil from holes in a damaged pipe. High-dose exposures resulted when people consumed food containing the contaminated oil. Infants of exposed mothers had low birthweights and hyperpigmented skin and mucous membranes.

PCB exposure may lead to a particular skin condition called chloracne. Dioxin-like PCBs are likely the congeners responsible for chloracne development. However, its absence

does not rule out exposure to PCBs. Chloracne may also be caused by exposure to other substances such as dioxins and dibenzofurans.

Chloracne may present as cystic skin-colored lesions measuring between 1 and 10 millimeters, as well as multiple open comedones, or “blackheads.” These lesions can become inflamed and secondarily infected.

Chloracne typically develops weeks to months after exposure and may occur at any age. It has been reported in both acute high-dose exposures and longer-term occupational exposures.

Lesions most often appear on the face in areas such as the chin, around the eyes, and the cheeks. However, the extremities and trunk can be affected as well. Chloracne may be difficult to treat, and lesions can last for years or decades.

Hyperpigmentation is also associated with moderate to high exposure to PCBs, dioxin like PCBs, and dioxins among workers exposed in occupational settings.

Ocular effects may also be seen with PCB exposures. Workers exposed to airborne PCBs may develop eye irritation, tearing, or burning. Hypersecretion of eye glands, conjunctival pigmentation, and eyelid swelling have been observed in humans with occupational exposure to PCBs. Ocular effects tend to accompany chloracne, and they may develop or persist after the exposure has stopped, possibly due to accumulation of PCBs in skin fat.

The liver is the main site of PCB metabolism, and metabolites are excreted in the bile and urine. Exposure has been associated with elevated liver enzymes and other changes in the liver.

Elevations of aspartate aminotransferase or AST, alanine aminotransferase or ALT, alkaline phosphatase, or AP, lactate dehydrogenase or LDH, and glutamyl transpeptidase or GGT have been linked to PCB exposure.

In occupational exposures, people may develop asymptomatic liver enlargement. Ingestion exposures have also been associated with an increased incidence of chronic liver disease and cirrhosis.

Although many people who are exposed show no overt signs or symptoms, people with liver complications may experience nausea, vomiting, abdominal pain, anorexia, weight loss, and jaundice.

PCBs may also induce hepatic microsomal enzymes, which can affect the metabolism of certain therapeutic drugs or other chemicals.

Children of mothers exposed to high levels of PCBs have been found to demonstrate a variety of health effects in infancy and early childhood. In-utero PCB exposure is linked to lower birth weight as well as hyperpigmented skin and mucosa. Infants also have higher mortality due to liver toxicity.

Children of exposed mothers also had higher risk of developmental and neurobehavioral deficits. These include poorer performance on neurocognitive tests, with lower IQ scores and impaired visual recognition and memory.

Exposure has been linked to markers of fertility, although the clinical significance is unclear. Men exposed to PCBs and polychlorinated dibenzofurans, in-utero were found to have changes in semen quality, including abnormal sperm morphology and decreased motility. However, it is unknown whether these findings are linked to fertility

problems.

Higher consumption of PCB-contaminated fish has been associated with a higher risk of conception failure in men in one study, but this effect was not seen in women.

Some PCBs have shown androgen receptor antagonism in vitro, and population-based studies have shown an inverse association between serum PCB concentrations with circulating testosterone among men and women.

Dioxin-like congeners and highly chlorinated mixtures have been shown to cause cancer in experimental animals. Epidemiologic studies in humans have shown positive associations with certain types of cancer, but overall evidence has been largely inconsistent.

The International Agency for Research on Cancer or IARC has classified PCBs as carcinogenic to humans. The strongest association in humans that led to this classification was with malignant melanoma.

In the US, the Environmental Protection Agency or EPA has designated PCBs as probable human carcinogens.

The US Department of Health and Human Services also concluded that PCBs are reasonably anticipated to be carcinogenic in humans.

Many epidemiologic studies have shown positive associations between PCB exposure and the risk of malignant melanoma. This link was first seen among people with occupational exposures, as well as in general populations across multiple cohort and case-control studies. These findings led to the IARC’s 2013 classification of PCBs as carcinogenic to humans. However, subsequent meta-analyses have yielded less

consistent findings.

Non-Hodgkin lymphoma is also positively associated with exposure in multiple occupational and large population-based cohort studies as well as case-control studies. However, results across high-quality studies were inconsistent.

Breast cancer risk may be associated with exposure, although meta-analyses have revealed heterogeneous and inconsistent results. Stronger associations have been found with certain congeners, but not overall PCB exposure.

Other sporadic and inconsistent positive associations have been reported for gynecologic cancers, multiple myeloma, childhood acute lymphocytic leukemia, lung cancer, thyroid cancer, brain malignancies, prostate cancer, and GI malignancies, including gastric, hepatic, biliary tract, pancreatic, and colorectal.

Limited data from occupational exposures and animal studies suggest that PCBs may also affect the thyroid gland.

People with goiter in a cohort study were found to be more likely to have been exposed to PCBs and polychlorinated dibenzofurans.

Effects on thyroid hormones varied in the studies, and their clinical significance is unclear. Some studies demonstrate an inverse association of triiodothyronine, or T-3, and thyroxine, or T-4 with PCBs.

Exposure is also associated with insulin resistance and the development of type 2 diabetes mellitus in multiple observational studies. Among nondiabetics, serum levels of nondioxin-like PCBs were positively associated with a homeostasis model assessment of insulin resistance.

PCBs may be either estrogenic or anti-estrogenic depending on the congener, eliciting responses via multiple mechanisms. The specific effects on estrogen receptors may depend on the congeners involved.

PCBs may cause immunosuppression and increased susceptibility to infections in children.

Now that we have discussed sources of PCBs, routes of exposure, populations at risk, and health effects, we will highlight aspects of clinical evaluation.

When evaluating a patient who may have been exposed, it is important to take a comprehensive occupational and environmental exposure history. The interview should emphasize past and present opportunities for exposure.

When assessing the past medical history, ask about skin lesions, history of hepatitis, other liver disease, cancer, developmental history, and gynecologic history.

Current health symptoms that may point to PCB exposure include headache and dizziness. Patients with liver toxicity may experience symptoms such as nausea, vomiting, abdominal pain, loss of appetite, weight loss, and jaundice.

On physical exam there may be skin findings of chloracne and hyperpigmentation as well as eye findings such as gland hypersecretion, conjunctival pigmentation, and eyelid swelling.

It is important to ask patients about occupational exposures. This includes any work involving the manufacture of PCBs and PCB-containing products, as well as repair,

maintenance, or recycling of any PCB containing equipment. People who work in waste disposal and other occupations may be at higher risk of exposure as well.

Workers in old buildings with old construction materials containing PCBs may also at risk for exposure.

Whenever possible, assess for the source of exposure as well as the intensity of exposure. Relevant questions include the use of personal protective equipment, when the exposure occurred on the job, and for how long.

Other activities outside the workplace may also increase the risk of exposure. Certain hobbies, such as those involving electronics, may result in exposure.

Environmental exposures may occur among people who are exposed to PCB containing materials in hazardous waste sites, or those who spend long periods of time in old buildings that contain PCBs in building materials.

Someone who lives in the same household as a person who is exposed to PCBs in the workplace may be exposed from contaminated clothing or shoes brought into the home.

Questions to assess for dietary sources of exposure include asking about consumption of fish or game from PCB contaminated areas.

The physical examination should focus on major organs and systems that PCBs may affect, including the skin, thyroid, heart, lungs, breasts, liver, and the nervous system.

PCB levels can be measured in serum by gas chromatography and mass spectrometry. Testing may be available through some commercial diagnostic labs. However, the clinical utility of these tests is limited. The results are often difficult to interpret, and no

known consistent causal associations exist between serum levels and specific adverse health effects.

PCB level testing is not recommended for routine evaluation of patients who report possible exposure. However, in select cases of suspected excessive acute or chronic exposures, testing may be helpful to confirm the exposure. Serum levels can be compared to CDC's national biomonitoring results.

Some diagnostic testing may be helpful for exposed patients, although this should be guided by the history and physical.

Consider checking serum liver enzymes, with subsequent testing only if indicated. For example, they may be helpful for patients with a known history of extensive exposure, or those with potential for ongoing exposure. In patients with elevated liver enzymes, rule out other causes of liver disease including infectious agents, autoimmune disease, rare genetic conditions, and other causes.

Biopsy of skin lesions may help diagnose chloracne.

Next, we will describe the treatment and follow-up of patients exposed to PCBs.
There is no specific antidote for acute or chronic PCB exposure. Treatment is mainly supportive.

The first priority is to remove the patient from the source of exposure. Remove any contaminated clothing and discard properly.

Patients with inhalation exposures should be observed for systemic symptoms and treated as necessary. There are no specific measures that can reduce PCB absorption via the respiratory tract.

As with acute exposures, the first consideration in chronic exposures is to remove the patient from the exposure environment if possible. There is no known prophylactic treatment to prevent development or progression of PCB related health effects.

Treatment of chloracne is based on stopping the exposure and practicing good skin hygiene. Chloracne can be difficult to treat. Lesions can become secondarily infected by bacteria, and antibiotics may be needed.

Consider referral to a dermatologist to develop a treatment plan for further management.

Periodic clinical evaluations of patients exposed to PCBs may detect abnormalities at an early stage, if they occur. Further testing may be performed based on symptoms, physical exam findings, and standard clinical practice.

There are no authoritative recommendations for screening tests to detect health outcomes related to PCB exposure. General screening for cancer and other chronic diseases should be performed in accordance with recommendations of the US Preventive Services Task Force or USPSTF based on age, gender, and other risk factors.

Consider consulting a specialist in occupational and environmental medicine to develop a plan for periodic monitoring if needed.

Now we will go over patient counseling and risk reduction.
To reduce the risk of exposure, patients should be encouraged to exercise caution when working with old electrical equipment that may be damaged. Encourage the use of administrative controls such as reducing exposure time for employees as well as work

practice controls including appropriate hygiene when working in areas containing PCBs. It is important to advise patients to wear appropriate gloves and other personal protective equipment when working with materials known to contain PCBs. When working in enclosed spaces, air ventilation should be increased.

Instruct people living near hazardous waste sites to avoid physical contact with soil and other potentially contaminated materials. Advise parents and guardians to prevent children from playing near waste sites.

Instruct patients to not consume fish or shellfish from waters contaminated with PCBs. Educate patients to check local, state, tribal, and federal fish consumption advisories. The U.S. Food & Drug Administration or FDA and EPA publish advice about eating fish for people who are or might become pregnant. Fish consumption during pregnancy is recommended, as fish provides many nutrients important for development. People who are or might become pregnant should be encouraged to choose “best choices” from FDA or EPA species lists, varying their fish sources, and choosing short-lived fish low on the food chain. Following these guidelines allows for the benefits of fish consumption while minimizing the risk for effects from PCBs or other contaminants.

Let’s discuss important takeaways from this presentation.
Chloracne, hyperpigmentation, and ocular effects may be overt signs of PCB exposure.

PCBs are associated with malignant melanoma and possibly other cancers such as non-Hodgkin lymphoma and breast cancer.

Treatment is mainly supportive with emphasis on removing patients from exposure.

Counseling measures may include proper protective equipment when working with materials containing PCBs and making safe choices with fish consumption.

For more information or questions, please contact the Environmental Medicine and Health Systems Intervention Section at ceatsdr@cdc.gov or CDC at 1-800-CDCINFO Teletypewriter: 1-888-232-6348 or www.cdc.gov.