

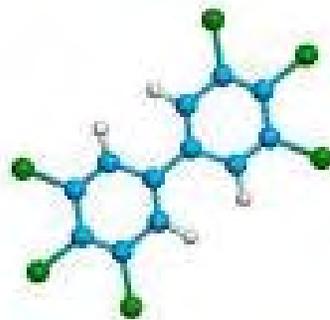
Polychlorinated Biphenyls (PCBs)

Kenneth Spaeth, MD, MPH

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Overview

- Background
- Distribution
- Sources
- Routes of Exposure
- Toxicokinetics
- Health Effects
- Public Health Complexities of PCBs
- References



Background - What are PCBs?

History

- Historic industrial uses:
 - Coolants and insulating fluids for transformers and capacitors (especially fluorescent light fittings and electrical transformers)
 - Plasticizers in paints, rubber products, and cements
 - Adhesives, caulking, carbonless copy paper, floor finish, thermal insulation material, etc.
- Present in U.S. manufacturing from 1929 until 1976 when they were banned due to their persistence in both the environment and living organisms
- Banned by the Stockholm Convention on Persistent Organic Pollutants in 2001



Background - What are PCBs?

Physical Properties

- No known smell or taste; colorless to light yellow
- May exist as oily liquids, solids, or vapor in air
- Relatively water insoluble but lipid soluble

Chemical Properties

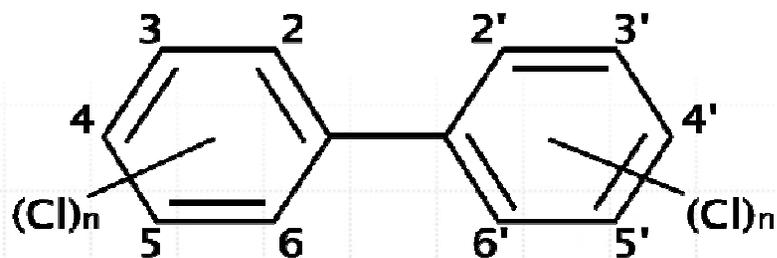
- Synthetic organochlorine chemicals
- Generally inert – resist acids & alkalis
- Thermal stability
- Non-volatile
- Relatively long half-life



Background – What are PCBs?

Chemical Properties Continued

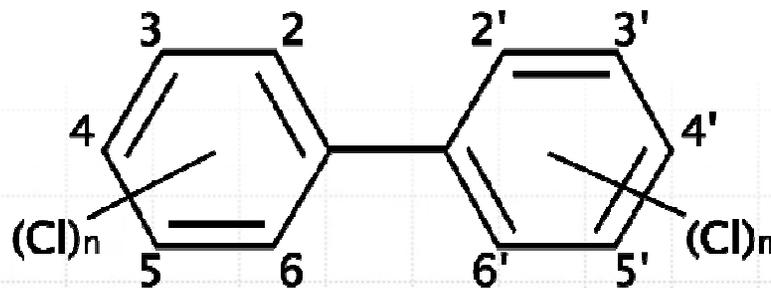
- Composed of:
 - The biphenyl molecule (two six-carbon rings linked by a single carbon-carbon bond)
 - Chlorine atoms – which can substitute hydrogen atoms at any of the 10 non-bonded positions on the biphenyl molecule
 - Position names:
 - Ortho: 2, 2', 6, and 6'
 - Meta: 3, 3', 5, and 5'
 - Para: 4 and 4'



Background – What are PCBs?

Chemical Properties Continued

- 209 individual PCB congeners can be formed
 - Differentiated by number of chlorine atoms and their location on the biphenyl rings
 - Two major congener structural classes:
 - Planar congeners: two benzene rings in the same plane
 - Dioxin-like properties and generally most toxic congeners
 - Non-planar congeners: two benzene rings are a 90 degree angle to each other



Background – What are PCBs?

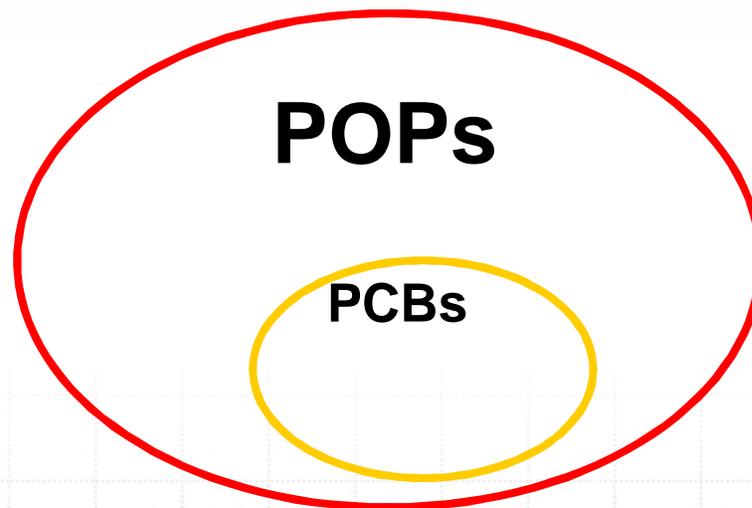
Mechanisms of Action:

- Biological mechanism of PCB health effects not completely understood
- Wide range of mechanisms of action depending on chlorine substitution pattern of congener
 - Estrogenic
 - Antiestrogenic
 - Neurotoxic
 - Dioxin-like

Background – What are PCBs?

Classification

- PCBs are part of a group of chemical substances known as Persistent Organic Pollutants (POPs)

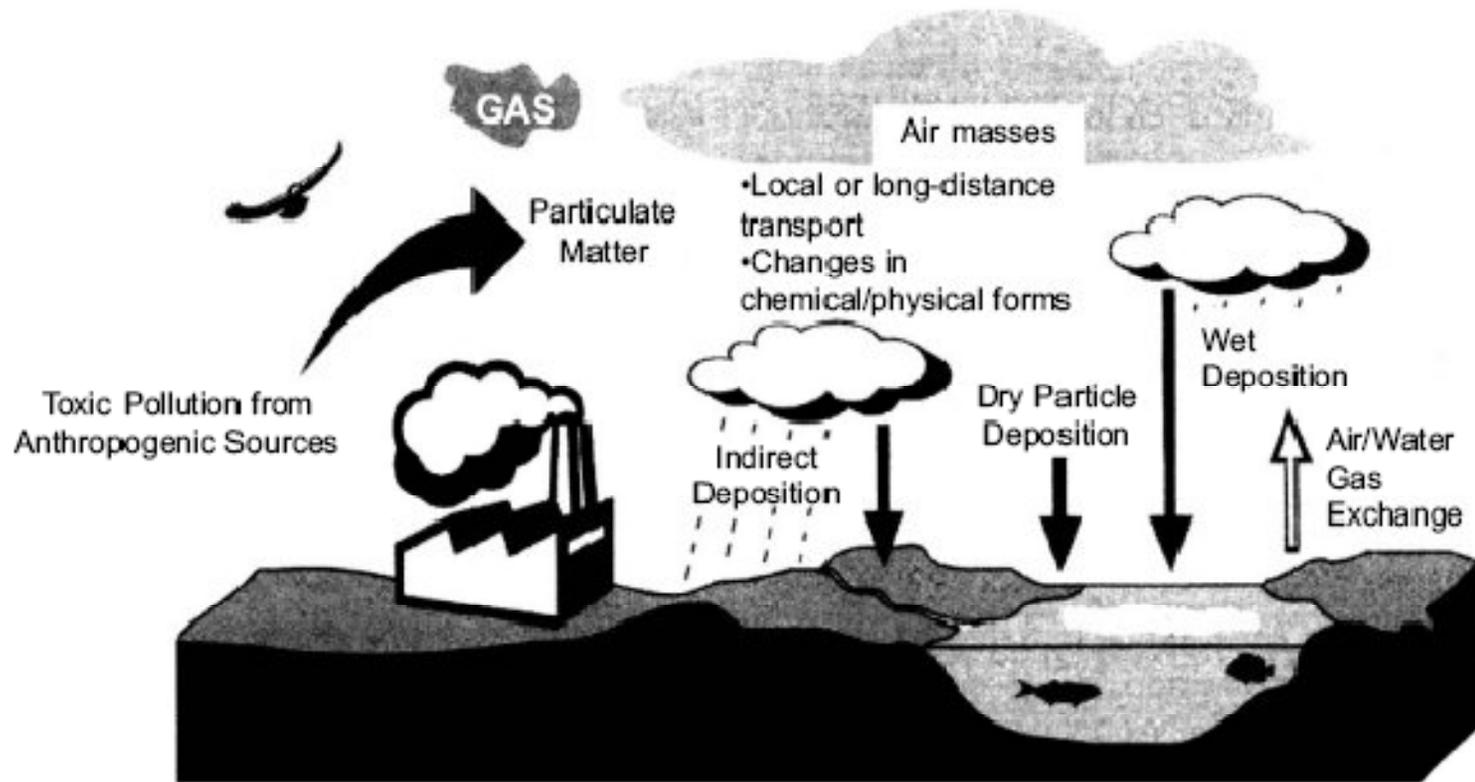


Background – What are PCBs?

Important characteristics of all POPs

- **Persistent:**
 - Resist usual forms of degradation (physical, chemical and biological)
 - Can remain for many decades in the environment
- **Bioaccumulative:**
 - Fat soluble - thus tend to accumulate in the body at much greater levels than found in the ambient environment
 - Can bioconcentrate up to levels 100,000x greater
- **Likely to have Adverse Health Effects:**
 - Humans, animals, & ecosystems
- **Distant contamination:**
 - Most are semi-volatile and can move anywhere on the planet
 - Wind currents
 - Water currents: ocean currents, rivers
 - Exposed species (i.e., birds, migratory mammals, etc.)

Distribution



•Adaptation from *Deposition of air pollutants to the Great Lakes (First Report to Congress)*, EPA, 1994. Included in the *World Federation of Public Health associations, Persistent Organic Pollutants and Human Health*, Washington,

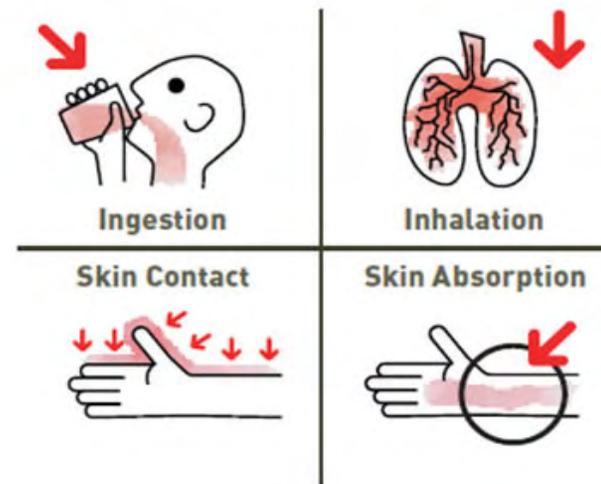
Sources

- No natural sources of PCBs
- Entered the environment during their manufacture, use, and disposal as a ***mixture*** of congeners and impurities
- Despite their banning, release of PCBs into the environment is ***still*** possible from:
 - Hazardous waste sites
 - Illegal/improper disposal of industrial wastes and consumer products
 - Leaks from old electrical transformers containing PCBs
 - Burning of some wastes in incinerators



Routes of Exposure

- All humans are exposed to PCBs on a daily basis
 - The question is not if there is exposure, but rather, how much?
- Ingestion
 - Assumed primary route
 - PCBs bioaccumulate in animal products, which may then be consumed by humans
 - May also accumulate in breast milk and be transmitted to infants through breast-feeding
- Inhalation
- Dermal absorption
- Three major pathways:
 - Environmental, accidental, and occupational



Toxicokinetics

- **Absorption:**
 - Absorbed readily in the gastrointestinal tract
 - Rate generally increases with extent of congener chlorination
 - Mechanism of absorption by the inhalation and dermal routes of exposure is unknown
- **Metabolism:**
 - Primarily hepatic metabolism
 - Rate of metabolism highly dependent on Cl substitution pattern of congener
 - Takes years, sometimes decades to clear
- **Storage**
 - Concentrate in adipose tissue due to lipophilic nature
- **PCB half-life in the human body**
 - Varies by congener and physiological processes of person
 - Ranges from a few years to ~20 years

Health Effects - Acute

Acute

- No reports of effects in humans following acute (short-term) exposure to PCBs are available
- Animal studies have reported acute effects on the liver, kidney, and central nervous system (CNS) from oral exposure to PCBs
- Acute animal tests in rats have shown PCBs to have moderate acute toxicity from oral exposure

Health Effects - Chronic

Systemic :

- Respiratory
- Cardiovascular
- Gastrointestinal
- Hematological
- Musculoskeletal
- Hepatic
- Renal
- Endocrine
- Dermal
- Ocular
- Body Weight

Immunological and Lymphoreticular

Neurological

Reproductive

Developmental

Genotoxic



Health Effects

Evidence for various PCB-associated diseases:

- Cancer:
 - PCBs are complete carcinogens and act as general cancer promoters
 - Assumed to increase risk for cancer of every kind
 - WHO – classified PCBs as “probable human carcinogens”
 - Types of cancers which studies have shown increased risk with PCB exposure:
 - Brain, Breast, Gastrointestinal, Liver/biliary, Lung, Malignant melanoma, Non-Hodgkin’s lymphoma, Thyroid, Prostate, Pancreatic

Health Effects

Evidence for various PCB-associated diseases:

- Recurrent Infections:
 - PCB exposure can suppress both the antibody and immune response
 - Human studies have shown exposure to PCBs results in great incidence in all types of infections:
 - Respiratory, skin, ear, measles, meningitis, chicken pox
- Neurobehavioral Effects:
 - In utero PCB exposure has been linked to:
 - Lower IQ and achievement tests
 - Low muscle tone and depressed reflexes
 - Poor performance on emotional and behavioral disorder measurement scales
 - Adult PCB exposure has been linked to loss of memory and IQ

Health Effects

Evidence for various PCB-associated diseases:

- Hypothyroidism:
 - Animal studies clearly show PCBs interfere with thyroid hormone at multiple sites
 - Human studies have shown relationship between PCB exposure and decreased thyroid function
- Infertility and Reproductive System Disorders
 - PCBs are potent inhibitors of the synthesis of testosterone
 - PCB exposure has been associated with:
 - In men: reduced sperm mobility; decreased testosterone levels
 - In women: earlier menarche; increased menstrual cycle length

Health Effects

Evidence for various PCB-associated diseases:

- Cardiovascular Disease and Elevated Serum Lipids:
 - PCB exposure associated with:
 - Higher plasma triglyceride levels
 - Higher serum cholesterol levels
 - Higher blood pressure
 - Increased CVD mortality
- Hypertension
 - PCB exposure associated with:
 - High blood pressure
 - Hypertension



Health Effects

Evidence for various PCB-associated diseases:

- Diabetes:
 - Dioxin exposure has been associated with elevated diabetes in multiple studies
 - Study with > 2,000 pregnant women showed dose-response relationship between PCB levels and diabetes
- Liver Disease
 - Several studies have found a positive association between serum PCB levels and elevated SGOT and GGTP
 - Studies by Fitzgerald et al. demonstrated that PCB exposure increases the rate of caffeine metabolism in the liver

Health Effects

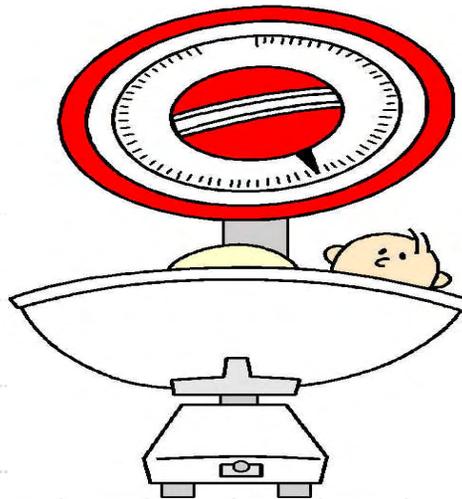
Evidence for various PCB-associated diseases:

- Asthma:
 - PCB exposure is associated with a significant increase in risk of asthma
 - Mechanism responsible is not known
- Arthritis
 - Studies have shown PCB exposure to be associated with joint disease and inflammation
 - A study of taiwanese men exposed to PCBs had elevated risk for developing arthritis and back problems due to intervertebral disc disease
 - Mechanism responsible is not known

Health Effects

Evidence for various PCB-associated diseases:

- Low Birth Weight:
 - Studies have shown maternal PCB exposure increases risk for giving birth to low birth weight babies
 - Apparent greater effect in males vs. females
 - Low birth weight associated with increased risk of several chronic diseases in adulthood (e.g., CVD, hypertension, and diabetes)



Public Health Complexities of PCBs

- Exposures are a PCB *mixture*
 - Each congener has its own profile of actions in biological systems
 - Without separation and quantification of individual PCB congeners during analysis, PCB concentrations can't be directly correlated to toxic equivalency
 - Toxicity of mixture may be influenced by chemical interactions
- Biomarkers are used for environmental exposure
 - Biomarkers: serum, blood, breast milk, adipose tissue, and human hair
 - Debate over equivalency of PCB levels in these different biomarkers
- Testing Issues
 - Lipid adjustment
 - Lack of standardized measurement procedure for human PCB levels
 - Random error
 - Questionable value of testing at all (there is no treatment)

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THANK YOU!

NS LIJ Occupational and Environmental Medicine Center

410 Lakeville Road

Lake Success, NY

(P) 516-465-5400



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