

TRAINING FOR THE HEALTH SECTOR



PERSISTENT ORGANIC POLLUTANTS (POPs)

Children's Health and the Environment CHEST Training Package for the Health Sector

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<<NOTE TO USER: Please add details of the date, time, place and sponsorship of the meeting for which you are using this presentation in the space indicated.>>

This module is based on the WHO module “Persistent Organic Pollutants”.

First draft prepared by: Drs T. Damstra & J. Pronczuk (WHO)

LEARNING OBJECTIVES

- ❖ To learn about POPs (persistent organic pollutants) and related substances
- ❖ To learn why and how POPs may affect children's health
- ❖ To identify gaps in knowledge and research needs
- ❖ To review international agreements and recommendations on POPs
- ❖ To discuss how health care providers and different stakeholders can take action to prevent exposure

<<READ SLIDE.>>

<<NOTE TO USER: Please add other objectives, if relevant, and refer to the situation of the country concerning the ratification of the Stockholm Convention and national implementation plans (NIPs).>>

WHAT ARE "POPs" ?

- ❖ **Synthetic organic chemicals**
- ❖ **Persistent in environment**
- ❖ **Long-range transport leads to global pollution**
- ❖ **Lipophilic**
- ❖ **Accumulate in food-chain**
- ❖ **High levels in fish and marine mammals**

Acute toxicity well-characterized



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The POPs are:

❖ **Synthetic (man-made) organic chemicals** – they are all synthetic chemicals, either intentionally or non-intentionally produced/released. Some are pesticides, others are industrial products or unintended by-products resulting from industrial processes or combustions (see next slide).

❖ **Persistent in the environment** – their persistence in the environment is remarkable – it may take them decennia or centuries to be degraded.

❖ **Long-range transport leads to global pollution** – Some POPs will almost always be found if tested for in tissues or environmental samples from different parts of the world. As is the case with many environmental pollutants, it is most difficult to establish that illness or disease are directly attributable to exposure to a specific persistent organic pollutant or to a group of POPs. This difficulty is further underscored by (a) the fact that POPs rarely occur as a single compound, and (b) that individual field studies are insufficient to provide compelling evidence of cause and effect in their own right.

❖ **Lipophilic** – they have a tendency to remain in fat-rich tissues. This affinity for the adipose tissues means that POPs are likely to accumulate, persist and bioconcentrate and could, eventually, achieve toxicologically relevant concentrations – even though exposure episodes may appear limited.

❖ **Accumulate in food-chain** – POPs enter into a cycle in nature, accumulating in the bigger animals as they eat the smaller ones.

❖ **Highest levels found in marine mammals** – immune dysfunction is considered as a plausible cause for increased mortality among marine mammals. It is postulated that the consumption by seals of fish contaminated with POPs may lead to vitamin and thyroid deficiencies and cause increased susceptibility to microbial infections and reproductive disorders.

❖ **Acute, high-level toxicity is well characterized** – acute effects after high-level exposure have been described for some of the organochlorine pesticides (e.g. aldrin, dieldrin and toxaphene). PCBs have caused well-documented episodes of mass poisoning called "Yusho" and "Yu Cheng", that occurred in China, Province of Taiwan, and in Japan. Pregnant women exposed had no or minor symptomatology, but their children presented adverse effects and developmental disorders. Some are potential endocrine disrupters – this will be addressed later in the presentation.

Ref: www.pops.int/documents/background/assessreport/en/ritteren.pdf

Picture above: NOAA, NURP, Wicklund. Humpback whales cruising beneath a diver.
www.photolib.noaa.gov/nurp/nur02001.htm

Picture below: NOAA, Captain Budd Christman. Humpback whale.
www.photolib.noaa.gov/animals/anim0800.htm

POPs and Children

PERSISTENT ORGANIC POLLUTANTS (POPs)

PESTICIDES

Aldrin
Dieldrin
Chlordane
DDT
Endrin
Heptachlor
Mirex
Toxaphene

INDUSTRIAL CHEMICALS

PCBs
HCB

UNINTENDED BY-PRODUCTS

Dibenzodioxins
Dibenzofurans

Stockholm Convention: a global treaty ratified by the international community led by UNEP – calls for the elimination and/or phasing out of 12 POPs

www.chem.unep.ch/pops/default.html

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These are the persistent organic pollutants – grouped according to their use and origin:

- 8 pesticides
- 2 industrial chemicals
- 2 unintended industrial by-products.

<<READ SLIDE.>>

PCBs: polychlorinated biphenyls

HCB: hexachlorocyclohexane

DDT: dichlorodiphenyl trichloroethane.

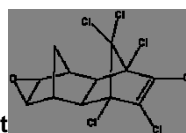
The Stockholm Convention is a global treaty ratified by the international community and led by the United Nations Environment Programme (UNEP) that calls for the elimination and/or phasing out of 12 POPs, called the "*dirty dozen*".

More information is available at: www.chem.unep.ch/pops/default.html

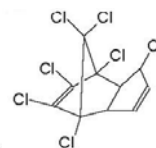
POPs and Children

POPs - PESTICIDES

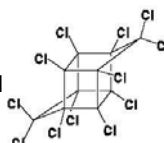
Endrin: White, odourless, crystalline solid (pure); light colour w/ faint chemical odour for technical grade



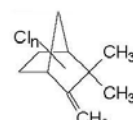
Heptachlor: White to light tan, waxy solid or crystals with a camphor-like odour



Mirex: White crystalline, odourless solid



Toxaphene: Yellow, waxy solid w/ chlorine/terpene-like odour



UNEP 5

•Endrin is a foliar insecticide used mainly on field crops such as cotton and grains. It has also been used as a rodenticide to control mice and voles. It is rapidly metabolized by animals and does not accumulate in fat to the same extent as other compounds with similar structures. It can enter the atmosphere by volatilization, and can contaminate surface water from soil run-off. The half-life of endrin in soil may be up to 12 years, depending on local conditions. This persistence, combined with a high partition coefficient (log KOW = 3.21–5.340), provides the necessary conditions for endrin to bioconcentrate in organisms. The chemical properties of endrin (low water solubility, high stability in the environment, and semi-volatility) favour its long-range transport, and it has been detected in arctic fresh water. The main source of endrin exposure to the general population is residues in food however, contemporary intake is generally below the acceptable daily intake of 0.0002 mg/kg body weight recommended by the Joint FAO/WHO Meeting on Pesticide Residues (JMPR).

•Heptachlor is a non-systemic stomach and contact insecticide, used primarily against soil insects and termites. It has also been used against cotton insects, grasshoppers, some crop pests and to combat malaria. Heptachlor is highly insoluble in water, and is soluble in organic solvents. It is quite volatile and can be expected to partition into the atmosphere as a result. It binds readily to aquatic sediments and bioconcentrates in the fat of living organisms. The half-life of heptachlor in temperate soil is up to 2 years. This persistence, combined with a high partition coefficient (KOW = 4.4–5.5), provides the necessary conditions for heptachlor to bioconcentrate in organisms. The chemical properties of heptachlor (low water solubility, high stability, and semi-volatility) favour its long range transport, and heptachlor and its epoxide have been detected in arctic air, water and organisms. WHO suggests that food is the major source of exposure of heptachlor to the general population. Heptachlor has been detected in the blood of cattle from both Australia and the USA. In both instances, heptachlor was among the most frequently detected organochlorine.

•Mirex is a stomach insecticide with little contact activity. Its main use was against fire ants in the southeastern United States, but it has also been used to combat leaf cutters in South America, harvester termites in South Africa, Western harvester ants in the USA, mealybug of pineapple in Hawaii and has been investigated for possible use against yellow jacket wasps in the USA. It has also been used as a fire retardant in plastics, rubber, paint paper and electrical goods. Mirex is very resistant to breakdown, is very insoluble in water and has been shown to bioaccumulate and biomagnify. Due to its insolubility, mirex binds strongly to aquatic sediments. Mirex is considered to be one of the most stable and persistent pesticides, with a half-life of up to 10 years. This persistence, combined with lipophilicity, provides the conditions necessary for mirex to bioconcentrate in organisms. The chemical properties of mirex (low water solubility, high lipid solubility, high stability, and semi-volatility) favour its long-range transport, and mirex has been detected in arctic fresh water and terrestrial organisms. The main route of exposure of mirex to the general population is through food, especially meat, fish and wild game, and intake is generally below established residue tolerances.

•Toxaphene is a nonsystemic and contact insecticide that was used primarily on cotton, cereal grains, fruits, nuts and vegetables. It has also been used to control ticks and mites in livestock. Toxaphene has been in use since 1949 and was the most widely used insecticide in the USA in 1975. Toxaphene is highly insoluble in water, and has a half-life in soil of up to 12 years. It has been shown to bioconcentrate in aquatic organisms and is known to undergo atmospheric transport. The half-life of toxaphene in soil ranges from 100 days up to 12 years, depending on the soil type and climate. This persistence, combined with a high partition coefficient (log KOW = 3.23–5.50) suggests that toxaphene is likely to bioconcentrate. The chemical properties of toxaphene (low water solubility, high stability and semi-volatility) favour its long-range transport, and toxaphene has been detected in arctic air. Exposure of the general population is most likely through food, however levels detected are generally below maximum residue limits.

These pesticides are banned and restricted in many countries, please see UNEP website for more information. *Notes and pictures taken from UNEP website: www.chem.unep.ch/pops/alts02.html*

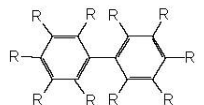
<<NOTE TO USER: The other POPs are addressed more in detail further on in the module.>>

POPs and Children

POPs – INDUSTRIAL CHEMICALS

PCBs: Polychlorinated biphenyls

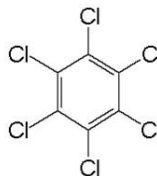
Trade Names for different mixtures (partial list): **Aroclor, Pyranol, Pyroclor, Phenochlor, Pyralene, Clophen, Elaol, Kanechlor, Santotherm, Fenchlor, Apirolio, Sovol**



UNEP

HCB: Hexachlorobenzene

White monoclinic crystals or crystalline solid



UNEP

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•Polychlorinated biphenyls (PCBs) are mixtures of chlorinated hydrocarbons that have been used extensively since 1930 in a variety of industrial uses, including as dielectrics in transformers and large capacitors, as heat exchange fluids, as paint additives, in carbonless copy paper and in plastics. There are 209 possible PCBs. PCBs in the environment may be expected to associate with the organic components of soils, sediments and biological tissues, or with dissolved organic carbon in aquatic systems, rather than being in solution in water. Association between elevated exposure to PCB mixtures and alterations in liver enzymes, hepatomegaly, and dermatological effects such as rashes and acne has been reported. Adverse effects are predominantly associated with higher blood concentrations. Contamination of rice oil by PCBs in Japan (1968) and China, Province of Taiwan (1979) has resulted in the exposure of a large number of people to PCBs and their contaminants PCDFs. Signs and symptoms of exposure from these incidents include enlargement and hyper secretion of the Meibomian glands of the eyes, swelling of the eyelids, and pigmentation of the nails and mucous membranes, occasionally associated with fatigue, nausea and vomiting. This was followed by hyperkeratosis and darkening of the skin with follicular enlargement and acneform eruptions, often with a secondary staphylococcal infection. Children born up to 7 years after maternal exposure in the Taiwan incident had hyperpigmentation, deformed nails and natal teeth, intrauterine growth delay, poorer cognitive development up to 7 years of age, behavioural problems and higher activity levels. The affected children appeared to "catch up" with controls at 12 years of age. Children born 7–12 years after maternal exposure experienced mildly delayed development, but no differences in behaviour. Effects observed in these children are probably a result of the persistence of PCBs in the human body, resulting in prenatal exposure long after the exposure took place. These effects are consistent with the observations of poorer short-term memory functioning in early childhood, in children exposed prenatally by mothers who had high consumption of Lake Michigan sports fish containing PCBs, amongst other POPs. People exposed in the Yucheng incident had low resistance, and suffered from a variety of infections. Examination during the first year revealed decreased concentrations of IgM and IgA, decreased percentages of total T-cells, active T-cells and helper T-cells, but normal percentages of B-cells and suppressor T-cells; suppression of delayed type response to recalling antigens; enhancement of spontaneous proliferation of lymphocytes and an enhancement in lymphoproliferation to certain mitogens. After 3 years, some, although not all, of the effects had disappeared. Cancer deaths in both male and female workers involved in the manufacture of electrical capacitors were significantly increased. A significant increase in haematological neoplasms and gastrointestinal cancers was observed in male workers. The persistence of PCBs, combined with the high partition coefficients of various isomers (log KOW ranging from 4.3 to 8.26) provide the necessary conditions for PCBs to bioaccumulate in organisms. Concentration factors in fish exposed to PCBs in their diet were lower than those for fish exposed to PCBs in water, suggesting that PCBs are bioconcentrated (taken up directly from the water) as opposed to being bioaccumulated (taken up by water and in food). The main source of PCB exposure to the general population is through food, especially fish.

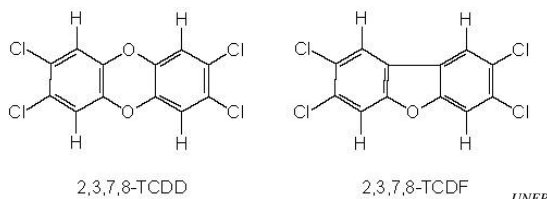
•Hexachlorobenzene (HCB) is a fungicide that was first introduced in 1945 for seed treatment, especially for control of bunt of wheat. HCB is also a byproduct of the manufacture of industrial chemicals including carbon tetrachloride, perchlorethylene, trichloroethylene and pentachlorobenzene. It is quite volatile and can be expected to partition into the atmosphere as a result. It is known to bioconcentrate in the fat of living organisms as a result. The most notable episode involving the effects of HCB on humans involved the ingestion of HCB-treated seed grain in eastern Turkey between 1954 and 1959. The patients who ingested the treated seed experienced a range of symptoms including photosensitive skin lesions, hyperpigmentation, hirsutism, colic, severe weakness, porphyrinuria, and debilitation. Approximately 3000–4000 people developed porphyria turcica, a disorder of haem biosynthesis. Mortality was up to 14%. Mothers who ingested the seeds passed the HCB to their children by placental transfer and through maternal milk. Children born to these women developed "pembe yara" or pink sore, with a reported mortality rate of approximately 95%. A study of 32 individuals 20 years after the outbreak showed that porphyria can persist years after the ingestion of HCB. HCB is very persistent. This persistence, combined with a high partition coefficient (log KOW = 3.03–6.42), provides the necessary conditions for HCB to bioconcentrate in organisms. The chemical properties of HCB favour its long-range transport, and HCB has been detected in arctic air, water and organisms. HCB is ubiquitous in the environment, and has been measured in foods of all types. HCB was one of two organochlorines detected in all samples of Spanish meat and meat products. These chemicals are banned and restricted in many countries, please see UNEP website for more information. *Notes and pictures taken from UNEP website: www.chem.unep.ch/pops/alts02.html*

<<NOTE TO USER: PCBs will be addressed more in detail further on in the module.>>

POPs –UNINTENDED BY-PRODUCTS

Dibenzodioxins and dibenzofurans

- ❖ By-products of production of other chemicals
- ❖ Detected in incineration of coal, peat, wood, hospital waste, hazardous waste, municipal waste, car emissions
- ❖ Of 210 dioxins and furans, 17 are in toxic mixtures



Polychlorinated dibenzo-*para*-dioxins (dioxins) and polychlorinated dibenzofurans (furans) are two groups of planar tricyclic compounds that have very similar chemical structures and properties. Their properties vary with the number of chlorine atoms present. Neither dioxins nor furans are produced commercially, and they have no known use. They are by-products resulting from the production of other chemicals. Dioxins may be released into the environment through the production of pesticides and other chlorinated substances. Furans are a major contaminant of PCBs. Both dioxins and furans are related to a variety of incineration reactions, and the synthesis and use of a variety of chemical products. Dioxins and furans have been detected in emissions from the incineration of hospital waste, municipal waste, hazardous waste, cars, and the incineration of coal, peat and wood. Of the 210 dioxins and furans, 17 contribute most significantly to the toxicity of mixtures.

At present, the only persistent effect associated with dioxin exposure in humans is chloracne. Other health effects that have been reported include peripheral neuropathies, fatigue, depression, personality changes, hepatitis, enlarged liver, abnormal enzyme levels and porphyria cutanea tarda though causal relationships were not established in every case.

Two recent studies followed a young population from the area of Seveso, Italy after an industrial accident. The first, a cancer study, examined a cohort of people aged 0–19 years living in the area at the time of the accident, for the period 1977–1986. Whereas a consistent tendency towards increased risk was apparent, none of the relative risks were significantly elevated. Non-significant increases in thyroid cancer and myeloid leukaemia were also observed. The study is limited, however, by the relatively short latency periods, the definition of exposure based on place of residence and the limited number of events. The second study examined the mortality of the same cohort of people for the same time period. Among those exposed, mortality owing to all causes did not deviate from expectations, however, as noted above, this study provides only limited evidence.

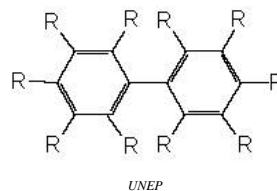
Dioxins and furans are considered to be very stable and persistent. This persistence, combined with high partition coefficients provides the necessary conditions for these compounds to bioconcentrate in organisms. The chemical properties of dioxins and furans (low water solubility, high stability and semi-volatility) favour their long range transport and these compounds have been detected in arctic organisms. As with most other organochlorines, food is a major source of dioxins and furans in the general population, with food of animal origin contributing the most to human body burdens.

Notes and picture taken from UNEP website: www.chem.unep.ch/pops/alts02.html

POPs and Children

EXAMPLES OF EFFECTS OF POPs ON WILDLIFE

- ❖ Reproductive impairment and malformations
- ❖ Immune system is sensitive
- ❖ Altered liver enzyme function
- ❖ Increased risk of tumours



- Mammals:** reproductive and immune effects in Baltic seals
Birds: eggshell thinning, gonadal and embryo alterations
Reptiles: decline in number of alligators
Fish: reproductive alterations
Snails: masculinization and population decrease (marine)

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The chlorination of biphenyl can lead to the replacement of 1–10 hydrogen atoms by chlorine; the conventional numbering of substituent positions is shown in the diagram.

The commercial production of the PCBs began in 1930.

They have been widely used in electrical equipment, and smaller volumes of PCBs are used as fire-resistant liquid in nominally closed systems. By the end of 1980, the total world production of PCBs was in excess of 1 million tonnes and, since then, production has continued in some countries. Despite increasing withdrawal from use, and restrictions on the production of PCBs, very large amounts of these compounds continue to be present in the environment, either in use or as waste.

In recent years, many industrialized countries have taken steps to control and restrict the flow of PCBs into the environment. The most influential force leading to these restrictions has probably been a 1973 recommendation from the Organisation for Economic Co-operation and Development (OECD) (WHO, 1976; IARC, 1978; OECD, 1982). Since then, the 24 OECD member countries have restricted the manufacture, sales, importation, exportation and use of PCBs, as well as establishing a labelling system for these compounds.

Current sources of PCB release include volatilization from landfills containing transformer, capacitor, and other PCB-containing wastes, sewage sludge, spills, and dredge spoils, and improper (or illegal) disposal in open areas.

Pollution may occur during the incineration of industrial and municipal waste. Most municipal incinerators are not effective in destroying PCBs. Explosions or overheating of transformers and capacitors may release significant amounts of PCBs into the local environment.

PCBs can be converted to PCDFs under pyrolytic conditions, at a temperature between 550 and 700 °C. Thus, the uncontrolled burning of PCBs can be an important source of hazardous PCDFs. It is therefore recommended that destruction of PCB-contaminated waste should be carefully controlled, especially with regard to the burning temperature (above 1000 °C), residence time, and turbulence.

Some examples of effects of exposure observed in wildlife are given in the slide:

Mammals: reproductive and immune effects in Baltic seals (PCBs, DDE).

Birds: eggshell thinning, altered gonadal development (DDT) and embryonic abnormalities (PCB).

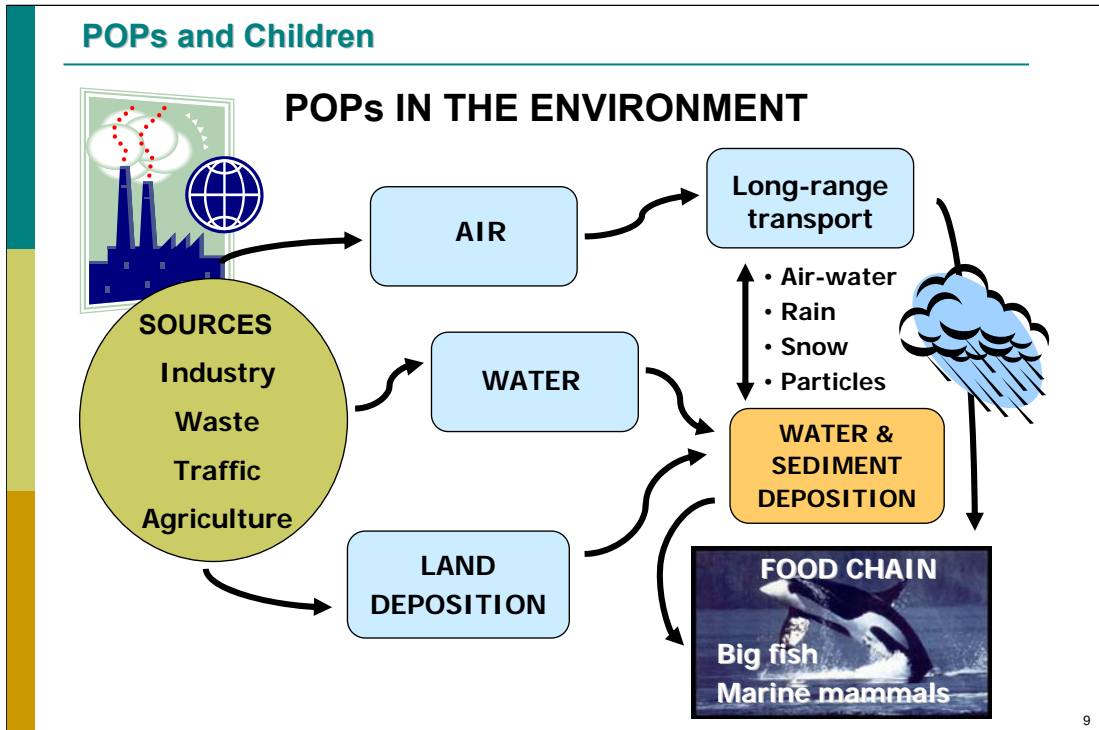
Reptiles: decline in alligators in Florida, USA (organochlorine spill).

Fish: reproductive alterations (from paper mills and sewage).

Invertebrates: masculinization and decreased population (TBT, a boat antifouling agent).

Picture: UNEP website: www.chem.unep.ch/pops/alts02.html

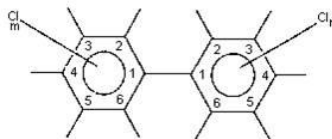
POPs and Children



- POPs have an anthropogenic origin: industrial processes, waste (e.g. medical), traffic and agriculture. A few may be of natural origin, e.g. from volcanic eruptions.
- POPs are released into air, water and land – from where they deposit into water, sediment, and enter the food-chain
- POPs are globally distributed through the air and ocean currents – they travel long distances and enter into atmospheric processes, air-water exchange and cycles involving rain, snow and dry particles. These processes lead to the exposure of even remote populations of humans and animals that depend on aquatic foods. Humans and animals are exposed mainly via ingestion of contaminated aquatic foodstuffs.
- POPs travel long distances and are found in places far away from industrial sites or from agricultural areas, such as the Arctic circle.

POPs and Children

AN EXAMPLE: PCBs



- ❖ **Widely used, released into the environment**
- ❖ **Caused mass-poisoning episodes**
- ❖ **Effects in animals: reproductive, immune, carcinogenic**
- ❖ **Effects in humans after high-level exposure:**
 - "Yusho" and "Yu-cheng" episodes
- ❖ **Effects of long-term, low-level exposures in children are a cause of concern...**

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•Polychlorinated biphenyls (PCBs) are very stable chemicals, with low volatility at normal temperature (non-volatile below 40°C), relatively fire-resistant and do not conduct electricity. PCB mixtures are usually light coloured liquids that look like molasses. PCBs are soluble in most organic solvents but are almost insoluble in water.

•They were used in a wide range of industrial and consumer products, especially in the oil of electric converters.

•Overheating of electrical equipment containing PCBs can produce emissions of irritating vapours.

•PCBs are completely destroyed only under extremely high temperatures (over 1100 °C!) or in the presence of certain combinations of chemical agents and heat.

•They are environmentally hazardous due to their extreme resistance to chemical and biological breakdown by natural processes in the environment.

•In the late 1960s the discovery of PCBs in birds in Sweden (by scientists researching DDT) and the outbreak of poisoning affecting 1200 people who had consumed rice oil contaminated with PCBs in Japan both focused public attention on the problem.

•PCBs have been released into the environment over the years, without any precautions, through open burning or incomplete incineration; by vaporization (from paints, coatings and plastics); by leakage into sewers and streams; by dumping in landfill sites, and by ocean dumping. Despite strict norms and regulations, PCBs may have been illegally dumped through ignorance, negligence or wilfully.

•The full health effects of PCBs on humans are unknown. It is unlikely that serious injury would result from short-term low-level exposure to PCBs. However, many are concerned about possible adverse health effects of long-term exposure to even low concentrations of these substances.

•PCBs can enter the body through skin contact, by the inhalation of vapours or by ingestion of food containing PCB residues. The most commonly observed health effect from *extensive* exposure to PCBs is chloracne, a painful and disfiguring skin condition, similar to adolescent acne. Liver damage can also result.

•When PCBs in transformers are involved in fires, particularly in buildings, the combustion of these materials can result in the production of highly toxic substances (chlorinated dibenzofurans and dioxins) thus increasing the hazard associated with smoke inhalation.

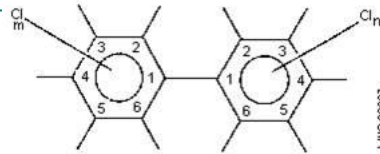
Experimental effects - PCBs produce a variety of effects ranging from the disruption of photosynthesis in microscopic plants, to effects on reproduction in higher animals. Marine/freshwater invertebrates, fish and birds are particularly sensitive to PCBs (effects include death of the embryo, abnormalities at birth). Long-term exposure can severely affect reproduction, PCBs are carcinogenic and have immunotoxic effects. In some species, liver toxicity has been reported.

Refs: Environment Canada - www.ec.gc.ca/pcb/pcb08/eng/pcb08ch16_e.htm

•www.atsdr.cdc.gov/DT/pcb007.html

POPs and Children

AN EXAMPLE: PCBs



❖ Effects in humans after high-level exposure:

- Skin rash, eyelid swelling
- Hyperpigmentation – CHLORACNE
- Headaches, vomiting

❖ Effects of long-term exposures:

- Hepato-, immuno-, reproductive and dermal toxicities

❖ Fetal exposures to PCBs:

- Neural and developmental changes
- Lower psychomotor scores
- Short-term memory and spatial learning effects
- Long-term effects on intellectual function

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Effects on humans - Although PCBs are widely recognized as a potential hazard to human health, the effects are not fully known. Brief exposure does not appear to be a major health hazard, but contact may cause skin rashes, swelling of eyelids, hyperpigmentation (the darkening of nails, skin and mucous membranes), headaches, or vomiting. Extended high-level exposure has resulted in cases of chloracne. The worst incident of human exposure was the 1968 Yusho incident: 1200 people (in Japan) consumed rice oil heavily contaminated with PCBs over 20 to 190 days. These people had reproductive dysfunction, severe chloracne, hyperpigmentation, eye discharges, headaches, vomiting, fever, visual disturbances and respiratory problems. Female victims tend to have disorders of the reproductive organs, and also an increased risk of miscarriage and stillbirth. Infants born to women who had been exposed to PCBs exhibited numerous effects, including neurobehavioural deficits and lower overall age-adjusted developmental scores were reported among the exposed children. The effects experienced were also attributed to polychlorinated dibenzofurans (PCDFs), considered more toxic than PCBs, a major contaminant of the PCBs. Some PCB mixtures are suspected human carcinogens (rats and mice may develop liver cancers), but no studies have yet been carried out to prove this. Similarly, the potential effects of PCBs on human reproduction have yet to be ascertained. The multigenerational effects of PCBs are still under study.

Refs:

- Environment Canada - www.ec.gc.ca/pcb/pcb08/eng/pcb08ch16_e.htm
- www.atsdr.cdc.gov/DT/pcb007.html

POPs and Children

PCB: HUMAN HEALTH INCIDENTS

Toxic effects at *high* levels of exposure, accidental or occupational:

- ❖ Dermal
- ❖ Ocular
- ❖ Blood and liver enzyme alteration
- ❖ Respiratory
- ❖ Immune system
- ❖ Neurological system
- ❖ Reproductive
- ❖ Developmental

"YUSHO" "YU-CHENG"

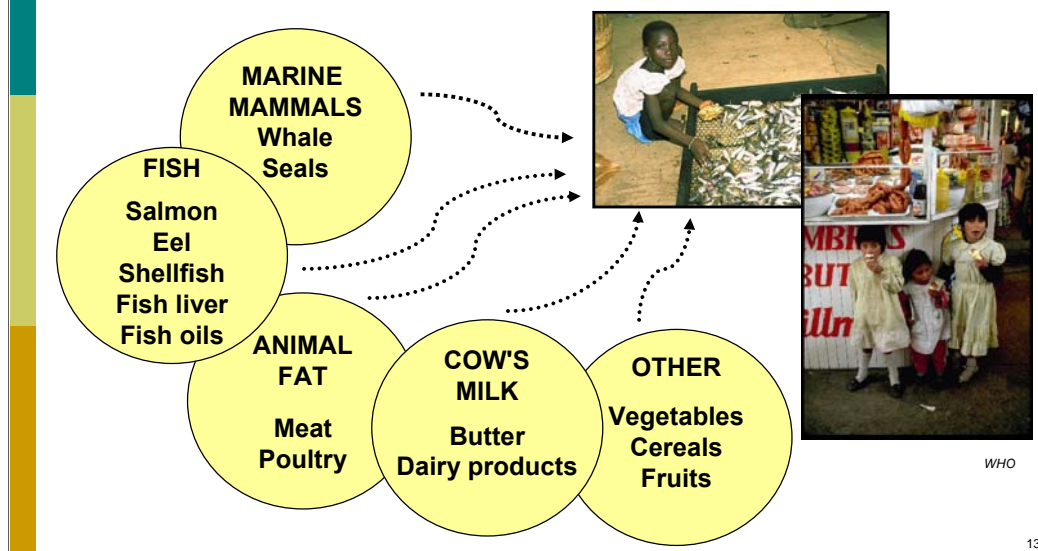
Adverse, persistent effects in newborns

- Low birth weight
- Reduced growth
- Hyperpigmentation
- Gingival hyperplasia
- Eye oedema
- Dentition at birth
- Skull calcifications

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- Two important mass-poisoning episodes have occurred: one in Japan ("Yusho") and one in China, Province of Taiwan ("Yu-Cheng").
- The main symptoms in Yusho and Yu-Cheng patients have frequently been attributed to contaminants in PCB mixtures, specifically, to PCDFs. Expert groups concluded that the symptoms may have been caused by the combined exposure to PCBs and PCDFs. However, some of the symptoms, principally, the chronic respiratory effects, may have been caused specifically by the methylsulfone metabolites of certain PCB congeners.
- The signs of intoxication in Yusho and Yu-Cheng patients included: eye irritation and lacrimation, swelling of the eyelids, hyperpigmentation of the nails and mucous membranes, occasionally associated with fatigue, nausea and vomiting. This was usually followed by hyperkeratosis and darkening of the skin with follicular enlargement and acneiform eruptions. Furthermore, oedema of the arms and legs, liver enlargement and liver disorders, central nervous system disturbances, respiratory problems (e.g. bronchitis-like) and changes in the immune status of the patients were also reported.
- Children of Yusho and Yu-Cheng patients presented: reduced growth, dark pigmentation of the skin and mucous membranes, gingival hyperplasia, xerophthalmia, oedematous eyes, dentition at birth, abnormal calcification of the skull, rocker bottom heel. A high incidence of low birth weight was reported.
- Infants born to women who had been exposed to PCBs exhibited numerous effects, including neurobehavioural deficits and lower overall age-adjusted developmental scores among the exposed children.
- The link between exposure and the occurrence of malignant neoplasms in these patients could not be definitely established, because the number of deaths was too small. However, a statistically significant increase in liver and lung cancer was observed in male patients, in the context of mortality due to all types of neoplasms (*Kuratsune, 1986*).
- Refs: www.atsdr.cdc.gov/DT/pcb007.html
- Kuratsune. Analysis of deaths seen among patients with Yusho, (Abstract FL17), In: *Dioxin 86, Proceedings of the VI International Symposium on Chlorinated Dioxins and Related Compounds, Fukuoka, Japan. 1986, p.179.*

MAIN ROUTE OF EXPOSURE TO PCBs: DIETARY



- As with many POPs, the main source of human exposure is dietary.
- Over the years, thousands of different food samples have been analysed, in several countries, for contaminants, including PCBs. Most samples have been from fish, meat and milk.
- Food becomes contaminated with PCBs through three main routes:
 - a) uptake from the environment by fish, birds, livestock (via food-chain), and also into crops;
 - b) migration from packaging materials into food (around 1 mg/kg, but in some cases up to 10 mg/kg);
 - c) direct contamination of foodstuff or animal feed as the result of an industrial accident or incident.
- The levels of PCBs found in different foodstuff are:
 - animal fat: 20 to 240 $\mu\text{g}/\text{kg}$;
 - cow's milk: 5 to 200 $\mu\text{g}/\text{kg}$;
 - butter: 30 to 80 $\mu\text{g}/\text{kg}$;
 - fish: 10 to 500 $\mu\text{g}/\text{kg}$, on a fat basis. Certain fish species (eel) and fish products (fish liver and fish oils) may contain much higher levels, up to 10 mg PCBs/kg;
 - vegetables, cereals, fruits, and a number of other products: <10 $\mu\text{g}/\text{kg}$.
- Main causes of concern regarding PCBs are: large fish, shellfish, marine mammals, meat, milk, and other dairy products. The median levels reported in fish, in various countries, are of the order of 100 $\mu\text{g}/\text{kg}$ (on a fat basis). However, it seems that the levels of PCBs in fish are slowly decreasing.

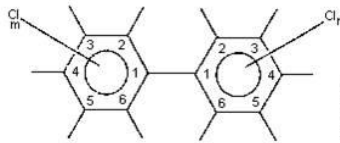
Refs: INCHEM. *Environmental Health Criteria 140, Polychlorinated Biphenyls and Terphenyls (Second Edition)*. Geneva, World Health Organization, 1993

•www.inchem.org/documents/ehc/ehc/ehc140.htm

Picture: WHO (Virot), Ghana, 2003.

POPs and Children

AN EXAMPLE: PCBs



- ❖ PCBs accumulate in human adipose tissue and breast milk
- ❖ In adipose tissue: <1 to 5 mg/kg, on fat basis
- ❖ Average concentration in human milk: 0.5 to 1.5 mg/kg fat
- ❖ PCB levels are higher in some areas or in relation to diet
- ❖ Concern: low-level exposures and neurodevelopment

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- PCBs accumulate in human adipose tissue and breast milk.
- The concentrations of PCBs in different organs and tissues depend upon the lipid content of the organ or tissue, with the exception of the brain.
- The levels of PCB residues in adipose tissue of the general population in industrialized countries range from <1 to 5 mg/kg, on a fat basis.
- The average concentration of total PCBs in human milk is in the range of 0.5 to 1.5 mg/kg fat, depending on the donor's place of residence, lifestyle, and the analytical methods used.
- Women living in heavily industrialized urban areas, or with a high fish consumption (especially fish from heavily contaminated waters), may have higher PCB concentrations in breast milk.
- Although PCBs are measurable, there are no agreed-upon methods, quality controls or reference values available. Thus far, all experts recommend breastfeeding and do not recommend testing of milk (AAP, 2003). "FOS does not have standard levels (of PCB in breast milk that may indicate interruption of breastfeeding) although the exposure of the infant is often over the current Provisional Tolerable Monthly Intake for dioxan-like PCBs. It is generally agreed that the benefits of breastfeeding would outweigh anything but the most acute type of health effects." (Dr G. Moy, WHO/SDE/FOS).
- Low-level exposures have been linked to neurodevelopmental effects in children. Prenatal exposure to low levels of PCBs (AAP, 2003):
 - Newborns: decrease in birth weight
 - Infants: motor delay detectable from newborn to age 2 years
 - 7-month-olds: defects in visual recognition memory
 - 42-month-olds: lower IQ (maybe some contribution from postnatal exposure)
 - 4-year-olds: defects in short-term memory
 - 11-year-olds: delays in cognitive development

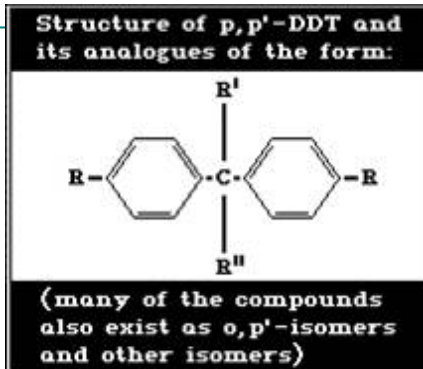
Refs: AAP. Polychlorinated biphenyls, dibenzofurans and dibenzodioxins. In: *Pediatric environmental health*, 2nd ed. Etzel R. ed. 2003.

• Environment Canada - www.ec.gc.ca/pcb/pcb08/eng/pcb08ch16_e.htm

POPs and Children

AN EXAMPLE: DDT

- ❖ Widely used in the past
- ❖ Malaria control in 12 countries!
- ❖ Adverse effects in animals
 - Reproductive, immune, neurological
 - Estrogenic and anti-androgenic effects
 - Liver effects and carcinogenesis
- ❖ Few studies on effects on children's health and development
- ❖ Exposure linked to preterm delivery, reduced birth weight and shortened lactation

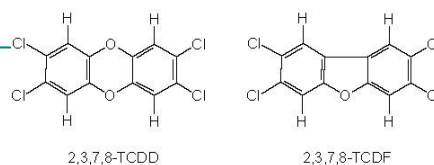


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- Dichlorodiphenyl trichloroethane (DDT) is a pesticide that was very widely used in the past. Although DDT is being banned worldwide, countries in sub-Saharan Africa have sought exemptions for malaria control.
- Adverse effects have been observed in animals – eggshell thinning and altered gonadal development have been observed in birds of prey exposed to DDT, resulting in severe population declines.
- Animal experimentation has demonstrated the effects of DDT on the liver and on the central nervous system, as well as estrogenic and antiandrogenic effects, and possible carcinogenicity
- Few studies have shown illness in children from the use of DDT. As a result, the risks of DDT exposure have been minimized. However, *plausible but inconclusive* data link DDT with more preterm delivery, small-for-gestational-age births and shorter duration of lactation. These studies raise the possibility that DDT does indeed have such toxicity. Assuming that these associations are causal, an increase in infant deaths might result from the use of DDT to combat malaria. The estimated increases in mortality could be of the same order of magnitude as the decreases from effective malaria control (*Chen and Rogan, 2003*). If maternal DDT exposure does in fact increase preterm births and decrease the duration of lactation, further investigation is warranted, especially in areas where DDT is reintroduced for malaria control. The unintended consequences of DDT use need to be part of the discussion of modern vector control policy.
- Although DDT can be found in adipose human tissue worldwide (and in breast milk), the levels of DDT and its metabolites are much higher in areas where it was used for malaria control.

Ref: Chen A, Rogan WJ. Nonmalarial infant deaths and DDT use for malaria control. *Emerg Infect Dis*, Aug 2003 (www.cdc.gov/ncidod/EID/vol9no8/03-0082.htm).

AN EXAMPLE: Dioxins



UNEP

- ❖ **Detectable in trace amounts in all parts of ecosystem**
- ❖ **Dioxins and furans: 210 compounds: 17 highly toxic**
 - **Seveso: release of high levels of dioxin in industrial accident (1976)**
 - **Considered one of the most toxic man-made compounds**
- ❖ **Sources in developing countries:**
 - **Production and use of chlor-organic chemicals**
 - **Pulp and paper industry**
- ❖ **Source in industrialized countries:**
 - **Combustion processes: waste incineration, iron and non-ferrous metal industry, ...**

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- Dioxins (PCDD) and furans (PCDF) are environmental contaminants detectable in trace amounts in air, water and soil.
- Typically, dioxins and furans are found in mixtures of about 210 compounds. 17 are highly toxic. One of these, known as Seveso dioxin, referring to the release of high levels of dioxin during an industrial accident in Italy in 1976, has been considered the most toxic man-made compound.
- They are produced worldwide and do not serve any purpose.
- In the past, environmental contamination due to dioxins and furans came primarily from production and use of chlor-organic chemicals. These included polychlorinated biphenyls, pentachlorophenol, and other chlorinated aromatic chemicals. The pulp and matter paper industry was a major source of contamination of the aquatic environment and still is in many developing countries.
- Today's major sources – at least in industrialized countries – are combustion processes of any type. Examples are: incineration of municipal, hazardous and clinical wastes, the iron and non-ferrous metal industry; and smaller sources, such as motor vehicles (especially when run on leaded petrol), home heating, open burning of waste and landfill fires.

Notes taken from UNEP website:

www.chem.unep.ch/pops/infosheets/is1-html/index.html

Picture: UNEP, www.chem.unep.ch/pops/alts02.html

POPs and Children

AN EXAMPLE: Dioxin – health effects

In humans:

- ❖ Chloracne
- ❖ Polyneuropathy
- ❖ Hepatomegaly
- ❖ Fatigue
- ❖ Depression
- ❖ Porphyria

IARC classification:
2,3,7,8-TCDD is a possible human carcinogen (Group 2B)

In animals:

- ❖ Chloracne
- ❖ Lymphatic alteration
- ❖ Liver effects
- ❖ Gastric lesion
- ❖ Epidermal lesions
- ❖ Chicken: oedema, ascites
- ❖ Rats: fetal death and resorption, endocrine alterations
- ❖ Mice: embryotoxicity, malformations

IARC classification: carcinogen

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•At present, the only persistent effect associated with dioxin exposure in humans is chloracne. Other health effects that have been reported include peripheral neuropathies, fatigue, depression, personality changes, hepatitis, enlarged liver, abnormal enzyme levels and porphyria cutanea tarda though causal relationships were not established in every case. Results of a study on 1520 workers known to have been exposed to 2,3,7,8-TCDD for a period of at least 1 year, and with a latency of at least 20 years between exposure and diagnosis of disease, revealed a slightly, but significantly elevated mortality from soft tissue sarcoma and cancers of the respiratory system. As with other studies, interpretation of results was limited by the small number of deaths and by possible confounders including smoking and other occupational exposures.

•Two recent studies followed a young population from the area of Seveso, Italy following an industrial accident. The first, a cancer study, examined a cohort of people aged 0–19 years living in the area at the time of the accident, for the period 1977–1986. Whereas a consistent tendency toward increased risk was apparent, none of the relative risks were significantly elevated. Non-significant increases in thyroid cancer and myeloid leukaemia were also observed. The study is limited, however, by the relatively short latency periods, the definition of exposure based on place of residence and the limited number of events. The second study examined the mortality of the same cohort of people for the same time period. Among those exposed, mortality owing to all causes did not deviate from expectations, however, as noted above, this study provides only limited evidence.

•In animals, effects of dioxin exposure that are common to most, and sometimes all, species include wasting, lymphoid involution, hepatotoxicity, chloracne and epidermal changes, and gastric lesions. Other characteristic responses include oedema and ascites in chickens; fetal death and resorption in rats and fetal wastage, embryotoxicity and malformations in mice.

Dioxins are associated with a variety of adverse effects on the reproductive systems of both male and female rats. Male reproductive toxicity has included altered regulation of luteinizing hormone secretion, reduced testicular steroidogenesis, reduced plasma androgen concentrations, reduced testis and accessory sex organ weights, abnormal testis morphology, decreased spermatogenesis, and reduced fertility. Signs of female reproductive toxicity included hormonal irregularities in the estrous cycle, reduced litter size and reduced fertility. IARC has concluded that while there is inadequate evidence for the carcinogenicity of 2,3,7,8-TCDD in humans, there is sufficient evidence in experimental animals. IARC has classified 2,3,7,8-TCDD as a possible human carcinogen (Group 2B).

As with most other organochlorines, food is a major source of dioxins and furans in the general population, with food of animal origin contributing the most to human body burdens.

Notes taken from UNEP website: www.chem.unep.ch/pops/alts02.html

<<NOTE TO USER: A reminder of IARC (International Agency for Research on Cancer) standard group classification:

1: "Carcinogenic to humans": there is enough evidence to conclude that it can cause cancer in humans.

2A: "Probably carcinogenic to humans": there is strong evidence that it can cause cancer in humans, but at present it is not conclusive.

2B: "Possibly carcinogenic to humans": there is some evidence that it can cause cancer in humans but at present it is far from conclusive.

3: "Unclassifiable as to carcinogenicity in humans": there is no evidence at present that it causes cancer in humans.

4: "Probably not carcinogenic to humans": there is strong evidence that it does not cause cancer in humans.>>

BEYOND THE "DIRTY DOZEN"...

- ❖ In addition to POPs, other chemicals are characterized by their persistence in the environment

Persistent Toxic Substances (PTSs)

- ❖ Can be transported long distances
- ❖ Can accumulate in organisms and enter food-chain
- ❖ Not "POPs" – not listed in the Stockholm Convention
- ❖ Could include: mercury, cadmium, lead, polybrominated diphenyl ethers (PBDE – flame retardants), others

<<NOTE TO USER: These are not POPs but it is foreseen that they will be included in further conventions or expanded international agreements.>>

- In addition to POPs, other chemicals are characterized by their persistence in the environment. They are called persistent toxic substances (PTSs) and may pose a serious threat to humans and the environment.
- They can remain in the environment for a long time and be transported long distances, far away from their site of origin.
- They can accumulate in organisms and enter the food-chain.
- Their levels in food may be of concern to human health.
- They are not "POPs" as they are not listed in the Stockholm Convention. However, there is growing concern that these chemicals, which are somehow *similar to the 12 listed in the UNEP convention*, may harm the environment, and through the environment, endanger human health.
- The list of PTS has not been defined, but could include, for example: mercury, cadmium, lead, the polybrominated diphenyl ethers (PBDE-flame retardants).

POPs and Children

BEYOND THE "DIRTY DOZEN"

Persistent Toxic Substances (PTSs) – Russian Arctic:

- ❖ **Indigenous people exposed to pesticides, industrial compounds, heavy metals**
- ❖ **Breast milk and umbilical cord blood have moderate to extremely high levels of PTS**
- ❖ **Why do PTS accumulate?**
 - **Northward flow in rivers, oceans and atmospheric currents**
 - **Low temperatures retard dispersal and degradation**

HCB
Dioxins
DDT
PCBs
Toxaphene
Mirex
HCH
Oxychlorodane
Mercury
Cadmium
Lead
PBDEs

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This slide illustrates a concrete example of POPs and PTSs found in a remote indigenous population, where a number of adverse health effects were found.

The yellow box shows some of the chemicals that were identified in a study of indigenous people living in the Russian Arctic areas.

Some are POPs (HCB, dioxins, DDT, PCB, toxaphene, mirex) and others are considered PTSs (those in bold).

Preliminary evidence from a study by the Arctic Monitoring and Assessment Program (AMAP) suggests that exposure to some persistent toxicants (PCBs, HCH, DDT, lead, cadmium and mercury) may be linked to stillbirths, birth defects, low birth weight and spontaneous abortions observed in some indigenous population groups. The study suggests an association between high blood lead levels and PCB exposure in pregnant women and reduced number of male births. In 1997–1998 the AMAP clearly documented that PTSs -primarily POPs – can be transported to, and accumulate in, the Arctic Region. Due to low solubility in water and high solubility in lipids, they can accumulate in fat-rich Arctic foodstuffs. As a result, certain Arctic indigenous populations, whose traditional diet is based on consumption of these food species, are subject to some of the highest exposure levels. These exposures may cause adverse health effects: neurological, reproductive, immunosuppression, cancer, and others. Due to the ability of some of these substances to cross the placenta and accumulate in breast milk, the fetus, newborns and infants may be exposed during critical periods of development.

HCB: hexachlorobenzene/HCH: hexachlorocyclohexane/PCBs: polychlorinated biphenyls/DDT: dichlorodiphenyltrichloroethane/PBDEs: polybrominated diphenyl ethers

Refs: Webster. Persistent toxic substances: study finds heavy contamination across vast Russian Arctic. *Science*, 2004, 306:1875.

•www.amap.no

POPs and Children

BEYOND THE "DIRTY DOZEN"

Semi-persistent organic pollutants



Corra, Ceppi

PAHs
Phthalate esters
PBDEs
PCNs
BPA
Alkylphenols

Found in sewage, generated by waste incineration and traffic

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A growing number of chemicals are now recognized as persistent or semi-persistent in the environment – they are found in sewage and may originate from waste or traffic, among other sources.

There is no general agreement on the terminology to be used for these substances, but in the future they may be included under the PTS. The list includes, for example:

- **PAHs** – polycyclic aromatic hydrocarbons. The high-molecular-weight molecules originate mainly from vehicle exhaust, and the lower-molecular-weight PAHs from low-temperature combustion, from fossil fuels (e.g. diesel), and spillage from ships and boats (Mai, 2003).
- **Phthalate esters** – used as plasticizers in polyvinyl chloride (PVC) products to make them soft. In 1999, the EU placed bans on these phthalates in toys and child care articles. The main phthalates are: DEHP, DBP, BBP, DINP, DIDP and DNOP (Hileman, 2004).
- **PBDEs** – polybrominated diphenyl ethers.
- **PCNs** – polychlorinated naphthalenes.
- **BPA (bisphenol A)** – high-volume production chemical used in the synthesis of polycarbonates and epoxy resins found in plastic bottles and in the lining of food cans. Small amounts may migrate into food. Reports suggest it may be estrogenic in animals and may have effects on the thyroid. (Kamrin, 2004, Zoeller, 2004).
- **Alkyl phenols** – widely used in industrial and domestic detergents as a surfactant, also used as an antioxidant for polymer resin, wall and floor coverings. They are found in sewage wastewater and also in the indoor air of newly built houses.

Refs: Hileman. Toys in phtalates. *Chemical and Engineering News*, 2004, 82 (40).

• Kamrin. Bisphenol a: a scientific evaluation. *Med Gen Med*, 2004, 6:7.

• Mai. Distribution of polycyclic aromatic hydrocarbons in the coastal region off Macao, China: assessment of input sources and transport pathways using compositional analysis. *Environ Sci Technol*, 2003, 37:4855.

• Zoeller. Bisphenol-A, an environmental contaminant that acts as a thyroid hormone receptor antagonist in vitro, increases serum thyroxine and alters RC3/neurogranin expression in the developing rat brain. *Endocrinology*, 2005, 146:607.

Picture: L. Corra and R. Ceppi. Argentina.

WHY IS THERE CONCERN ABOUT CHILDREN?

- ❖ Special vulnerability of children and developing fetus
- ❖ Effects depend upon dose and timing of exposure
- ❖ Some POPs are endocrine disrupters
- ❖ Effects are exacerbated by adverse environmental and social conditions – (e.g. poverty, poor diet,...)

•Although the special susceptibility of children has been known for decades (every paediatrician knows it!) it is only in the last decade that this vulnerability has been NEWLY recognized. Children are more vulnerable because of their physiology (organs and systems are growing and maturing; they eat and drink more), their behaviours (hand-to-mouth, spending time near the ground/soil, and their ignorance of danger (do not read labels, do not recognize dangers). In addition, they are politically powerless and cannot protect themselves.

<<NOTE TO SPEAKER: THE NEXT SLIDES REFER TO THE SPECIAL VULNERABILITY OF CHILDREN, TIMING OF EXPOSURE, BODY BURDEN AND ENDOCRINE DISRUPTION – PLEASE SELECT THOSE OF RELEVANCE TO THE AUDIENCE.>>

•There is NEW knowledge about the importance of dose and TIMING of exposure, because of the special "windows of vulnerability" – periods of development when the effects of a toxicant have important consequences. The importance of the TIMING of exposure is now recognized (see next slide).

•Special concern exists about the potential for endocrine disruption in children – as will be seen later on in the presentation.

In the more degraded environments, the adverse effects are exacerbated or magnified. Poverty may force people to live in polluted sites and eat contaminated foodstuffs. Malnutrition, ignorance and stress may predispose to exposure and adverse effects on health.

WHY IS THERE CONCERN ABOUT CHILDREN?

- ❖ Exposure through unique routes { Transplacental
Breast milk
- ❖ During critical developmental processes
"Windows of susceptibility"
- ❖ Immature metabolic pathways
- ❖ Effects may appear later in life
- ❖ Body burden is acquired early in life

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In the case of children, there is special concern for several reasons, as stated in the previous slide. There are other reasons:

❖ Increased exposures may occur through specific routes, that are UNIQUE to children:

- Transplacental – most of the child's exposure through the mother occurs *in utero*.
- Breast milk – many of the POPs have been found in breast milk, raising controversies concerning the desirability of breastfeeding.

<<NOTE TO SPEAKER: Stress that WHO strongly supports breastfeeding – and that some research has demonstrated that "contaminated" human milk has a more positive effect on the growth and development of small children than non-contaminated artificial formula.>>

❖ During critical developmental processes: "Windows of susceptibility" (as already stated).

❖ Immature metabolic pathways may increase, in some instances, the levels and effects of exposure to toxicants.

❖ POPs start accumulating very early in life – even *in utero* – and the body burden may increase throughout the years.

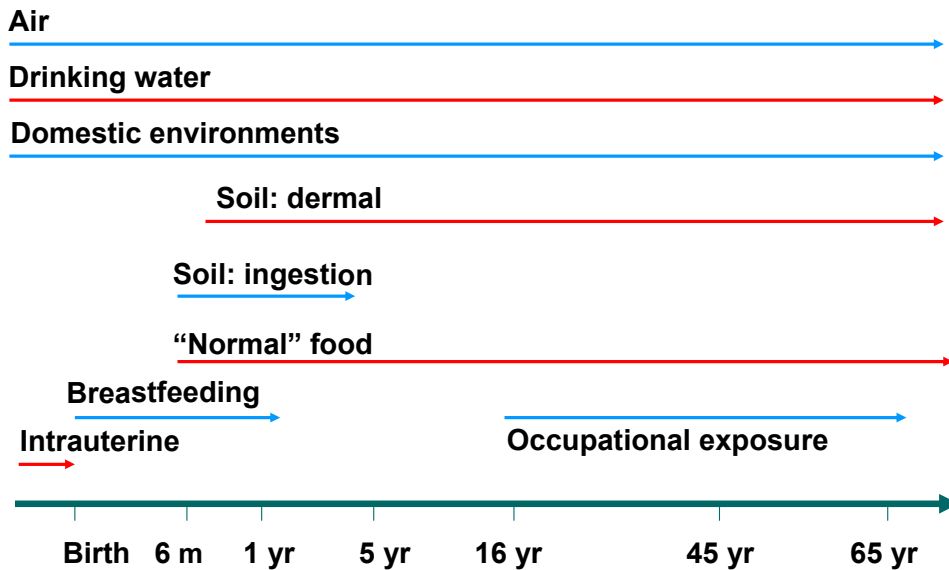
❖ Effects may become apparent long after exposure, during adulthood, for example.

Refs:

- Pronczuk. Guest editorial: Breast milk: An optimal food. *EHP*, 2004, 112:A722.
- Van Leeuwen. Results of the third round of WHO-coordinated exposure study on the levels of PCBs, PCDDs and PCDFs in human milk. *Organohalogen Compounds*, 2002, 56:311.

POPs and Children

LIFETIME EXPOSURES



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- This diagram helps to explain how the body burden of POPs (and other chemicals...) builds through lifetime exposures.
- It may start *in utero*, through the mother's exposure to POPs in food or air.
- After birth, exposure occurs first through breastfeeding (up to 12–18 months, in general) and afterwards, through contamination in solid foods that are usually introduced after 6 months.
- The toddler spends much time on the floor, and may be exposed to contaminated soil – through skin or because of ingestion.
- Occupational exposure starts later in life – usually after late adolescence.
- Contaminated air, water and indoor environments contribute to the body burden throughout life.

TIMING OF EXPOSURE – A MOST CRITICAL FACTOR

During “fetal programming”: permanent changes

During adulthood: homeostasis compensates

During different life stages: different effects

Timing of exposure determines: type and severity of effects

- Exposure during the “programming“ period in the fetal stage may result in permanent changes.
- Exposure during adulthood tends to be compensated by homeostasis and may not result in detectable effects.
- Exposure to the same level during different life stages may produce different effects.
- Timing of exposure will determine *both* the nature and severity of effects.

SOME POPS ARE ALSO ENDOCRINE DISRUPTERS

- ❖ **Endocrine system – crucial to child's growth and development**
 - **Nutritional, behavioural and reproductive processes**
 - **Growth, gut, cardiovascular and kidney functions**
 - **Responses to all forms of stress**
- ❖ **"Hormones": neurohormones, intercellular and intracellular chemical regulators (cytokines and intracines)**
- ❖ **Hormonal disorders – *overactive and under- active hormone secretion* – may result in disease**

The endocrine system is crucial to children's growth and development. Their nutritional, behavioural and reproductive processes are regulated by hormones, as are their growth, gut, cardiovascular and kidney functions, and responses to all forms of stress.

The concept of "hormone" has been broadened by the discovery of chemical regulators secreted by neurones (neurohormones), intercellular and intracellular chemical regulators (cytokines and intracines) all of which may also be affected by endocrine disrupting chemicals (EDCs).

The disorders of the endocrine system – overactive and underactive hormone secretion – may result in disease.

EDCs are natural or synthetic hormones and plant constituents, and also synthetic chemicals (e.g. some pesticides, industrial by-products, and chemicals used in plastics) that have the potential to interfere with the endocrine system.

ENDOCRINE DISRUPTING CHEMICALS (EDCs)

Exogenous substance/mixture that alters the function(s) of the hormonal system and consequently causes adverse effects in an intact *organism*, or its *progeny* or its *subpopulation*

❖ EDCs may *natural* or *synthetic*

❖ Effects

- **Functional change** – not a "toxic end-point"
- **Direct or indirect**
- **Complex: multiple mechanisms of action**

<<READ SLIDE>>

Endocrine disrupting chemicals (EDCs) were defined by the EDC-IPCS Working Group as: "exogenous substance or mixture that alters the function(s) of the hormonal system and consequently causes adverse effects in an intact organism, or its progeny or its subpopulation".

The substances may be of *natural* or *synthetic* origin.

An example of EDCs of natural origin is the "phytoestrogens" present in plants.

The synthetic ones include some pesticides, industrial by-products, chemicals used in plastics, pharmaceuticals that enter the natural environment, and persistent organic pollutants (POPs) (addressed in the next slides).

The potential effects are FUNCTIONAL and not a toxic end-point.

These functional changes *may or may not* lead to an adverse event.

It is difficult to distinguish between the direct and indirect effects and to distinguish the primary from the secondary effects.

The effects are complex as they result from multiple mechanisms of action on a hormonal system with close interconnections and "cross-talk".

POPs and Children

SOME EFFECTS OF EDCs (POPs in red)

- Estrogenic **DDT, dieldrin**, endosulfan, methoxychlor, **PCBs**, alkylphenols, phthalates, mycotoxins, phytoestrogens
- Anti-estrogenic **Dioxins, PCBs**, phytoestrogens
- Anti-androgenic **DDT**, vinclozolin
- Anti-thyroid **PCBs, dioxins**
- Anti-progestins **PCBs, DDT**

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This slide illustrates the complexity of effects that may be caused by different chemicals, and the fact that the same chemical may have different effects.

For example, DDT may have estrogenic, anti-estrogenic or anti-progestin effects.

Phytoestrogens may be both estrogenic and anti-estrogenic.

<<READ SLIDE.>>

WHY IS THERE CONCERN ABOUT EDCs?

- ❖ Reproductive/developmental effects observed in wildlife
- ❖ Effects demonstrated experimentally, in animals
- ❖ Increasing trends of hormone-related cancers
- ❖ Neurobehavioural deficits in children

The existing concern about endocrine disrupting chemicals – some of which are POPs – is due to several observations:

- Reproductive/developmental effects have been observed in wildlife.
- Similar effects have been demonstrated in animal experimentation.
- Epidemiological studies and reports show an increasing trend of hormone-related cancers (e.g. breast, prostate, testicular,...).
- Neurobehavioural deficits in children are reported with increasing frequency and it has been postulated that they may be connected with endocrine-related developmental effects (e.g. effects on the thyroid).

MORE CONCERNS ABOUT CHILDREN AND EDCs

- ❖ Neurobehavioural and cognitive impairment
- ❖ Impaired immune function
- ❖ Altered sex ratio (fewer males)
- ❖ Increased incidence of malformations
 - **Hypospadias, cryptorchidism**
- ❖ Low birth weight
- ❖ Precocious puberty

All of the following have been linked to endocrine-disrupting effects:

- ❖ Neurobehavioural and cognitive impairment
- ❖ Impaired immune function
- ❖ Altered sex ratio (fewer males)
- ❖ Increased incidence of malformations
 - hypospadias, cryptorchidism
- ❖ Low birth weight
- ❖ Precocious puberty

KEY QUESTIONS:

How do we identify POPs and their effects on children's health and development?

May environmental exposures affect children's growth and development?

If so, do environmental exposures result in limited school attendance and reduced intellectual performance in children?

What is the magnitude of the problem due to POPs with endocrine-disrupting effects in children?

How do we identify persistent environmental pollutants and their effects on children's health and development?

Are the environmental exposures affecting children's growth and development?

Do they limit the school attendance and the intellectual performance of girls and boys?

What is the magnitude of the problem due to exposure to EDCs in children?

NEW KNOWLEDGE IS DIFFICULT TO GENERATE

- ❖ Endocrine effects are functional (not a toxic end-point!)
- ❖ Effects occur at several sites
- ❖ Effects occur through various mechanisms
- ❖ There is *developmental* sensitivity – particular risks for:
 - "programming" of the fetus
 - child's development
- ❖ Information on exposure is very limited

There are numerous knowledge gaps, and they are difficult to fill. Why?
Because:

- Endocrine effects are functional – the effects are not a toxic end-point per se or a lesion, but a dysfunction that is difficult to diagnose.
- Effects occur at many sites in the organism.
- Effects occur through several mechanisms – receptor-mediated responses include the binding of the hormone to its receptor at the cell surface, cytoplasm or nucleus, followed by a complex series of events that lead to changes in gene expression characteristic for a specific hormone. Changes in gene expression represent an early and critical step in the regulation of normal biological functions (e.g. cell proliferation and differentiation).
- *Developmental* sensitivity leads to particular risks for:
 - "programming" of the fetus; and
 - children's development.
- Information on exposure is very limited in all countries, especially in the developing ones.

RESEARCH NEEDS IDENTIFIED

- ❖ **Systems to study mechanisms of action of POPs and EDCs**
- ❖ **Chemical and biological analytical methods to measure POPs and assess endocrine disruption**
- ❖ **Monitoring the exposure of the fetus and developing child**
- ❖ **Risk management: reducing the use and release of EDCs**
 - **Industrial, municipal and medical waste**
 - **Good agricultural practices for pesticides**

Some of the research needs identified are as follows:

1. Bioassay systems to study mechanisms of action in relation to specific chemicals and mixtures.
 - Finding out which chemicals are responsible for adverse effects.
2. Chemical and biological analytical methods, that should be cost-effective, for measuring POPs in different media and also for measuring EDCs.
3. Monitoring the exposure of the fetus and developing child.
 - New methodologies to measure exposure and effects.
 - Determining exposure in susceptible human groups, including children.
4. Risk management: reducing the use and release of EDCs.
 - Treatment and disposal of industrial, municipal and medical waste.
 - Good agricultural practices in the use and disposal of pesticides.

CHALLENGES FOR THE HEALTH CARE PROVIDER

- ❖ Which children are/may be exposed to high levels of POPs?
- ❖ How do we reduce exposure?
- ❖ How do we change diet and lifestyle habits?

Improving the paediatric environmental history:

- ❖ Type of diet? (Wild game? Sport fish? Other?)
- ❖ Place where children live?
- ❖ Learning difficulties?
- ❖ Child's development?

<<READ SLIDE>>

Ref:

- Abelsohn. Identifying and managing adverse environmental health effects: 5. Persistent organic pollutants. *CMAJ*, 2002, 166 (www.cmaj.ca/cgi/content/full/166/9/1161).

PREVENTION

- ❖ **Most fish are nutritious.... Some may have contaminants**
→ *Seek local fish advisories*
- ❖ **Improve fish cleaning and cooking methods**
→ *Removing fat*
- ❖ **Advocate elimination of POPs from industrial sources, waste incineration and power generation**
- ❖ **Request cleaning of contaminated sites and sediments**



WHO

Corra, Ceppi

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<<READ SLIDE>>

Ref:

- Abelsohn. Identifying and managing adverse environmental health effects: 5. Persistent organic pollutants. *CMAJ*, 2002, 166 (www.cmaj.ca/cgi/content/full/166/9/1161).

Picture above: WHO/PAHO, J. Vizcarra.

Picture below: L. Corra and R. Ceppi. Argentina, Sante Fé.

THE WAY AHEAD...

- ❖ Promote international, collaborative research on POPs
- ❖ Build health and environment partnerships for action
- ❖ Advocate the elimination of POPs and the support of the Stockholm Convention



www.chem.unep.ch/pops/

<<READ SLIDE>>

Ref:

- Damstra. Persistent organic pollutants: potential health effects?
Journal of Epidemiology and Community Health, 2002, 52:824.

OVERALL CONCLUSIONS ABOUT EDCs

- ❖ **Certain environmental chemicals (*some of which are POPs*) may interfere with endocrine processes, affecting growth and development**
- ❖ **Effects in wildlife have been demonstrated**
- ❖ **Data on EDCs and *human* health effects are not conclusive – but the "weight-of-evidence" approach indicates a potential for adverse outcomes – especially in children**
- ❖ **The potential health effects warrant *global* concern**
- ❖ **Coordinated international research strategies will help address numerous gaps and uncertainties in the data**

Certain chemicals present in the environment may interfere with endocrine processes, particularly those affecting growth and development.

There are sufficient data to conclude that adverse endocrine-mediated effects have occurred in wildlife.

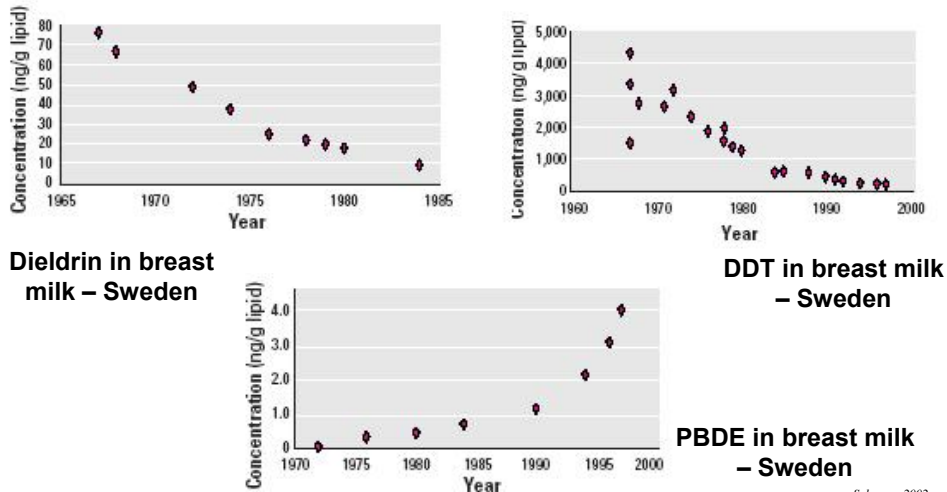
Although data on EDCs and human health effects are scarce, overall the "weight-of-evidence" approach indicates the potential for adverse outcomes – especially in children.

The potential health effects and their repercussions in the future of both developed and developing countries warrant global concern.

Coordinated international research strategies involving both industrialized and developing countries are urgently needed to address numerous gaps and uncertainties in the data.

POPs and Children

POPS IN BREAST MILK An example on the efficacy of interventions



Solomon, 2002 37

- Research on environmentally-related chemical contaminants in milk has been going on for several decades in several countries. Exposure varies according to local chemical use and different diets.

- Breast milk contamination is an important indicator of environmental and public health problems. Many of the POPs (organochlorine pesticides, PCBs and dioxins) have decreased in the countries that have placed bans on their use and production. However, levels of PBDEs are rising.

- When dieldrin and aldrin became internationally used, their levels in breast milk rose dramatically. As countries banned their use, the prevalence of detection remained high, but levels in breast milk dropped significantly. In Sweden, as seen on the figure on the left of the slide, there has been a clear decrease in average levels of Dieldrin in breast milk over several decades.

- Use of DDT in Sweden was restricted in 1970 and banned in 1975. We can see in the figure on the right how the levels of DDT in breast milk declined in direct correlation with the time since its restriction. Other countries where studies have revealed a decrease in the levels over the years include Canada, China, Hong Kong, Special Administrative Region, the Czech Republic, Denmark, India, Israel, Japan, Norway, Switzerland, Turkey, the United Kingdom and Yugoslavia.

- PBDEs came into use as flame retardants and are used in carpets, furniture cushions and construction materials. They may affect hormone function and may be toxic to the developing brain. PBDEs have been associated with non-Hodgkin lymphoma in humans, cancer in rodents and disruptions of thyroid hormone balance. Mothers exposed to PBDEs pass the suspected neurotoxicant to their unborn children. In the figure at the bottom of the slide we can see that the concentrations of PBDE in breast milk in Sweden show a logarithmic increase.

Clearly, restrictions and bans do work, but the problem remains as new threats come "out of the woods".

PCBs: polychlorinated biphenyls.

DDT: dichlorodiphenyltrichloroethane.

PBDEs: polybrominated diphenyl ethers.

Refs: Solomon. Chemical contaminants in breast milk: time trends and regional variability. *EHP*, 2002, 110: A339.

• Washam. Suspect inheritance: potential neurotoxicants passed to fetuses. *EHP*, 2003, 111: A480.

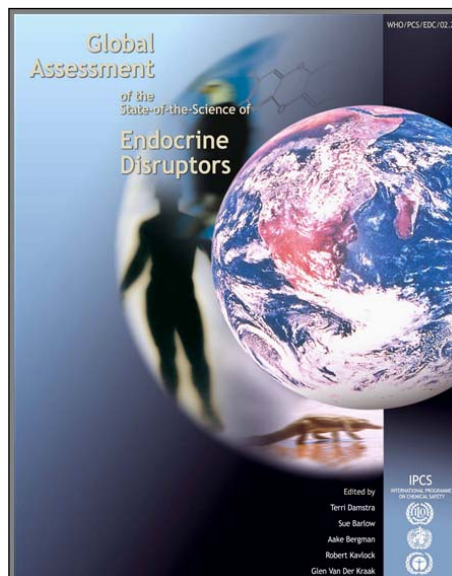
Figures: Solomon, Chemical contaminants in breast milk: time trends and regional variability. *EHP* (2002) 110 (6), A339. Reproduced with permission from *EHP*.

POPs and Children

Due to continuing concerns regarding EDCs, WHO/IPCS was requested to provide an objective state-of-the-science assessment

A global perspective was prepared by over 65 international scientific experts using the *weight-of-evidence* approach

www.who.int/pcs/emerg



www.who.int/pcs/publications/new_issues/endocrine_disruptors/en/

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<< READ SLIDE >>

<<NOTE TO USER: This publication may be requested free of charge from:

IPCS/WHO

Av. Appia 20

1211 Geneva 27

Switzerland.>>

PROTECTING CHILDREN'S HEALTH AND ENVIRONMENTS

Governments and stakeholders

- ❖ To recognize the importance of exposure to POPs
- ❖ To respond to international agreements
- ❖ To implement policies and take protective actions
- ❖ To promote health and environment collaboration

Health care providers

- ❖ To learn about POPs/EDCs and their potential threats
- ❖ To diagnose, prevent, treat and investigate
- ❖ To advocate for the protection of children

As children represent the future of our societies and have the right to healthier, cleaner and safer environments, the different sectors are called to join efforts and to work towards the protection of children from the potential effects of POPs and EDCs.

<<READ SLIDE.>>

<<NOTE TO USER: Describe the roles that the different sectors may be called to play in the country.>>

POPs and Children



WHO

Children represent the future of nations.

They need cleaner, safer and healthier environments – free of POPs and other pollutants.

Clean environments and education will enable children to reach their full potential as individuals, as contributing members of society and as pillars for sustainable development

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Prevention of exposure through cleaner, safer and healthier environments – free of persistent organic and other pollutants – is the single most effective means of protecting children against environmental threats.

Education about the environment and human health will enable our children to become informed individuals, contributing members in their own societies and promoters of sustainable development.

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