TRAINING FOR HEALTH CARE PROVIDERS

CHILDREN AND CHEMICALS

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.>>

This presentation deals with children and chemicals – an issue of great concern for parents and communities, and also for policy-makers, that has been the subject of a number of international recommendations, and where health care providers are called to play a key role.

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LEARNING OBJECTIVES

- Learn about chemical hazards – what they are and the risks they may pose to children
- Identify the scenarios – how, where and when are children exposed?
- Recognize signs, symptoms and diseases due to acute and chronic toxic exposures in children
- Know how to assess, prevent and treat children's toxic exposures

<<READ SLIDE>>

Children and Chemicals

- ❖ **Chemicals used in everyday life**
- ❖ **Risks and benefits**
- ❖ **Unwanted pollutants in the environment**

Exposures to chemicals in the micro- and macro-environments of children may cause functional and organic damage during periods of vulnerability

WHO

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<<READ SLIDE>>

Myriad chemicals are used in everyday life – they bring in numerous benefits,in protecting human and animal health, promoting hygiene, protecting crops, controlling vectors of disease.

But chemicals may also pose risks to human and animal health..

Many become unwanted pollutants and some of these are persistent!

Exposures to chemicals in the micro- and macro-environments of children may cause functional and organic damage, especially during periods of vulnerability.

Children and Chemicals

Chemicals and global environmental health issues

- ❖ **Household water insecurity**
- ❖ **Poor hygiene and sanitation**
- ❖ **Air pollution - indoor and outdoor**
- ❖ **Disease vectors**
- ❖ **Chemical hazards**
- ❖ **Injuries and accidents**
- ❖ ***…. EMERGING ISSUES!***

WHO 4

At the GLOBAL level, WHO has identified six main environmental threats to children's health, in addition to the so-called "emerging issues".

All of these threats have either a strong *chemical* component or are related to the use of chemicals. These threats are as follows:

•**Household water insecurity**. Although in developing countries the main concern is *microbiological* contamination, a number of water pollutants have a tremendous impact on public health, namely: arsenic, lead, fluoride and pesticides. In addition, water chlorination, recommended for drinking and recreational waters may bring in health problems as halogenated by-products are formed when chlorine interacts with organic matter.

•**Poor hygiene and sanitation**. These hinder the maintenance of clean environments – the washing, cleaning and removal of chemicals, dirt and pollutants. In some instances, where water is scarce, the maintenance of hygiene may call for extra use of chemical cleaners!

•**Air pollution (indoor and outdoor)**. Ozone, SO2, N02, sulfate particles (a major fraction of the particle burden in urban air), carbon soot, polycyclic aromatic hydrocarbons and carbon monoxide, are some of the typical air contaminants, whose effects on children's morbidity and mortality have been clearly demonstrated. Tobacco smoke is very rich in particles and polycyclic aromatic hydrocarbons. Indoor air pollution from use of biomass fuel in developing countries is a major public health problem, as it contributes heavily to the mortality of children under 5 years.

Ref: Schwartz, Air Pollution and Children's health, Pediatrics (2004) 113 (4): 1037

•**Disease vectors**. Combating malaria, dengue and other vector-borne diseases relies to a great extent on the use of pesticides, and this increases the risk of children's exposure to these products used either at home or in the context of public health campaigns

•**Chemical hazards**. Exposure to both the "old" and "new" chemicals, of anthropogenic and natural origin, present in the places where children spend time can be dangerous (this will be the theme of the presentation).

•**Injuries and accidents.** These include poisoning, the non-intentional (or intentional) injury due to toxicants (e.g. a child exploring the kitchen cupboard).

•**… EMERGING ISSUES!** These include the consideration of climate change, the ozone layer and also the potential risk posed by electromagnetic fields and by chemicals that persist in the environment (persistent organic pollutants (POPs)).

Ref:

•*IARC, Chlorinated drinking-water, chlorination by-products halogenated compounds; cobalt and cobalt compounds, IARC Monograph vol. 52, 1991*

Children and Chemicals

Children may suffer acute and/or chronic poisoning…

PAHO

❖ **HOUSEHOLD PRODUCTS**
- **Kerosene, solvents, cleaners, pesticides...**
- **Pharmaceuticals**
- **…inappropriate places and containers**

EPA

❖ **WASTE SITES**
- **Chemicals leak into soil and water**
- **Open burning releases dioxins, heavy metals and particles**
- **Scavengers**

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These are two typical examples of how exposure to toxicants may occur:

In the home environment, where the "little explorer" (usually a toddler) finds and "tests" the attractive containers in which the products such as solvents, cleaners, corrosive agents and pesticides may be stored.

In poor environments, where scavenging children spend long hours in waste sites becoming exposed to discarded chemicals, to fumes from burning rubbish, to vectors of disease and numerous other risk factors.

Children and Chemicals

Children are exposed to chemicals at home, in the school, the playground, fields and streets

In rural and urban environments, in:

- **Household products, building materials, house dust**
- **Pharmaceuticals, cosmetics, hygiene products and toys**
- **Workplace (of the parents...or the child!)**
- **As Persistent Organic Pollutants (POPs) in the environment**
- **As chemicals of natural origin:**
  - **As and Fl in water, aflatoxins, cyanide, pyrrolizidine alkaloids…**

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<<READ SLIDE>>

Children are exposed to myriad chemicals at home, at school, in the playground, in fields and streets;

Both in rural and urban environments.

<<NOTE TO USER: mention under each bullet, if appropriate, the examples that are relevant to the area. >>

Toxicants are present in or as:

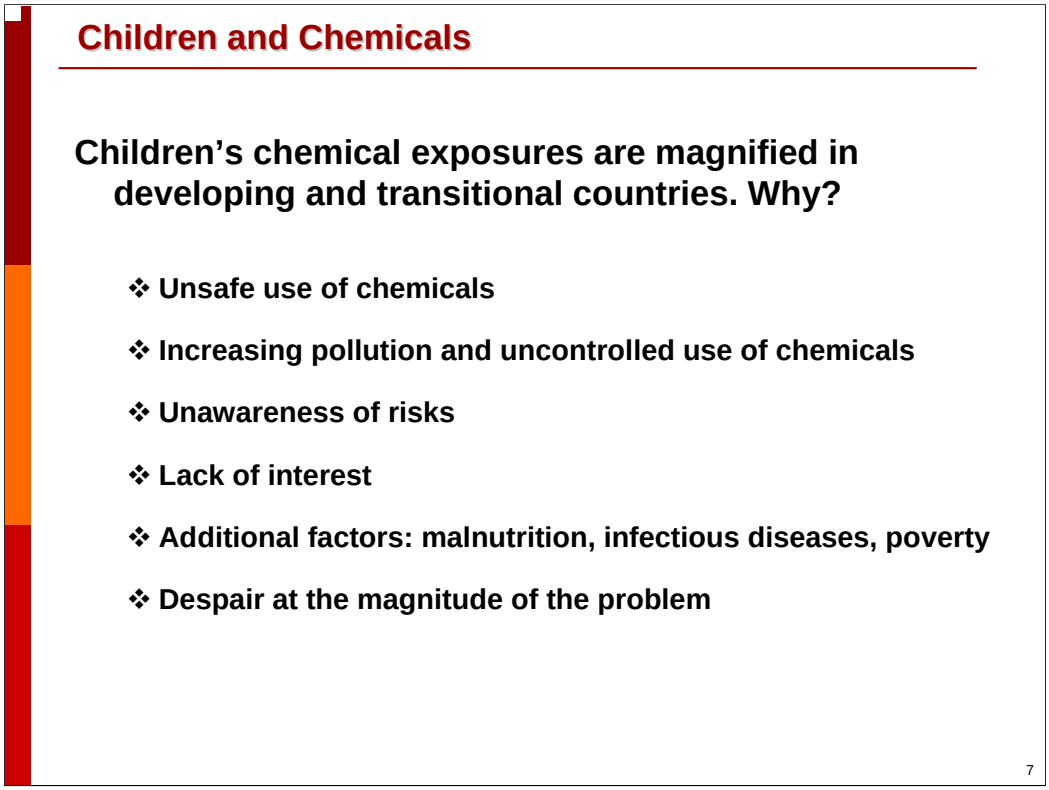
•household products, building materials and house dust;

•unexpected contaminants in pharmaceuticals, cosmetics, hygiene products and toys;

•persistent organic pollutants (POPs);

•chemicals in the workplace of the parents or the child; and also as "take home" exposures, e.g: when the working parent brings in contaminated clothes to the home.

•chemicals of natural origin: including arsenic (As) and fluorides (Fl) in water, mycotoxins (e.g. aflatoxins), cyanogen radicals (plants that are rich in cyanide-generating compounds, e.g. Cassava – used as staple food in many African countries) and pyrrolizidine alkaloids (present in some plants that may be used to prepare herbal teas).



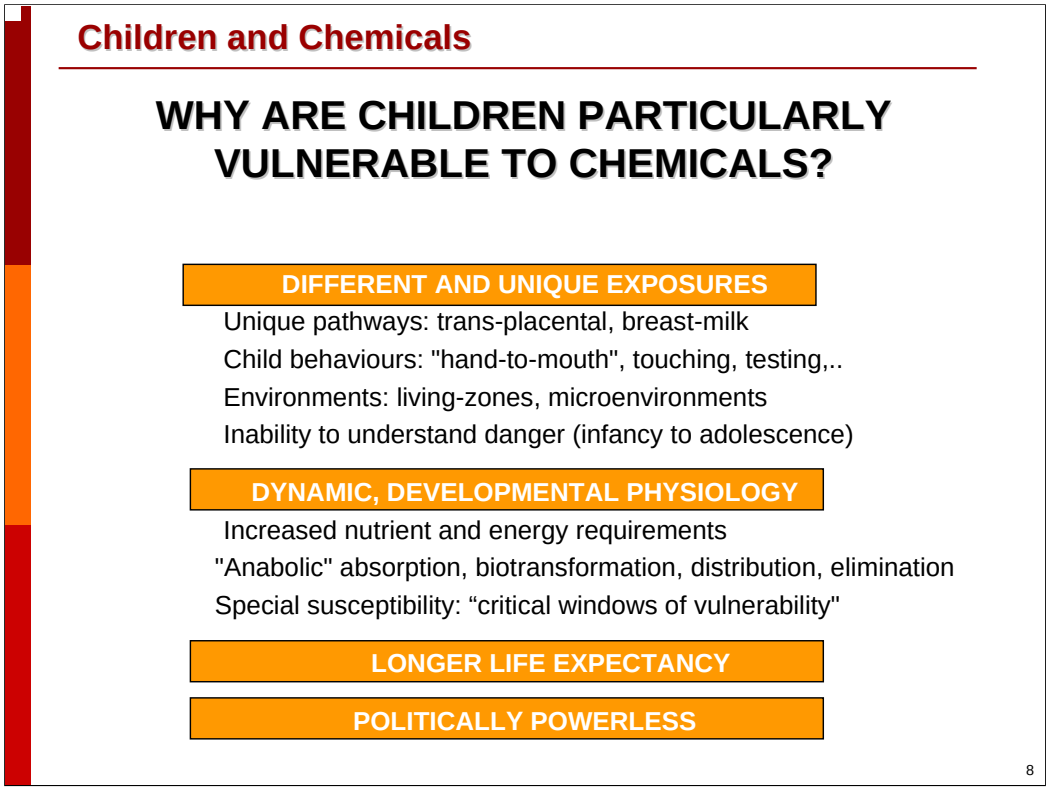
Children's environmental health and chemical safety problems are magnified in developing countries and countries in transition and in the poor parts of the world for reasons including the following:

- ❖unsafe use of chemicals – due to lack of information and education on their safe and judicious use and to prevailing illiteracy;
- ❖increasing pollution and uncontrolled use of chemicals – due to lack of appropriate regulatory measures or the impossibility of enforcing them (e.g. because of lack of personnel, controls and surveillance);
- ❖lack of awareness about risks and poor access to information;
- ❖lack of interest because of other urgent, immediate health priorities!
- ❖additional factors such as malnutrition, infectious diseases and poverty; and
- ❖despair at the magnitude of the problem, … that appears to be impossible to solve!

<<NOTE TO USER: if appropriate, provide examples relevant to the area, to illustrate the points made >>

Ref:

•*Goldman, Toxics and poverty: the impact of toxic susbtances on the poor in developing countries, Washington DC, The Wrold Bank, 2002.*



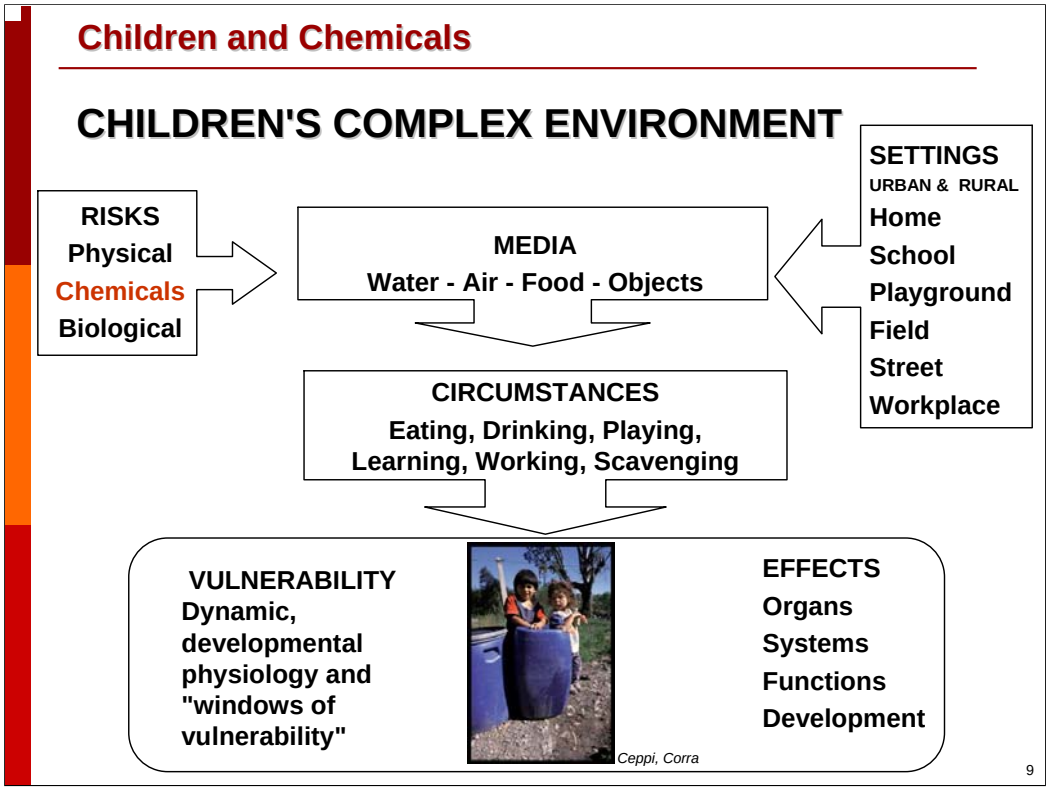
We now recognize that children, including the embryo, fetus, infant and all life stages until the completion of adolescence, are often at different and increased risk from environmental hazards from that of adults, for reasons that can be divided into four major categories.

1. Children often have different and sometimes unique exposures to environmental hazards from those of adults.

2. Due to their dynamic developmental physiology, they often receive higher exposures to pollutants found in air, water and food which may be handled quite differently by an immature set of systems from the ways they are dealt with in adults. Furthermore, the developmental component of a child’s physiology is changing, maturing, differentiating and growing in phases known as developmental windows. These critical windows of vulnerability have no parallel in adult physiology and create unique risks for children exposed to hazards which can alter normal function and structure.

3. Children have a longer life expectancy. They have longer to manifest disease with a long latency period, and longer to live with toxic damage.

4. Finally, children are politically powerless; they are defenceless. With no political standing of their own, they must rely on adults to protect them from toxic environmental agents. Each of these points is illustrated in more detail in the following series of slides.



This slide summarizes the way CHEMICALS present in the environment (as a risk) may reach the child through media (e.g. water, air, food and objects) and during activities such as eating, drinking, playing, learning or working (and scavenging, in poor areas...).

CHEMICALS are present in the places (settings) where children spend most time: including home, school, fields, playgrounds, streets – both in urban and rural areas.

Children of different age groups are affected because of their special vulnerability – they are developing very rapidly, need high levels of nutrients and energy, have an "anabolic" metabolism and special “windows of vulnerability” (as seen in the previous slide).

The effects of exposure to chemicals may have an impact on organs, which are developing, on systems and functions, which are maturing, and on the developmental process of growth.

Picture: Ceppi, Corra, Argentina. Used with permission.

POINTS FOR CONSIDERATION

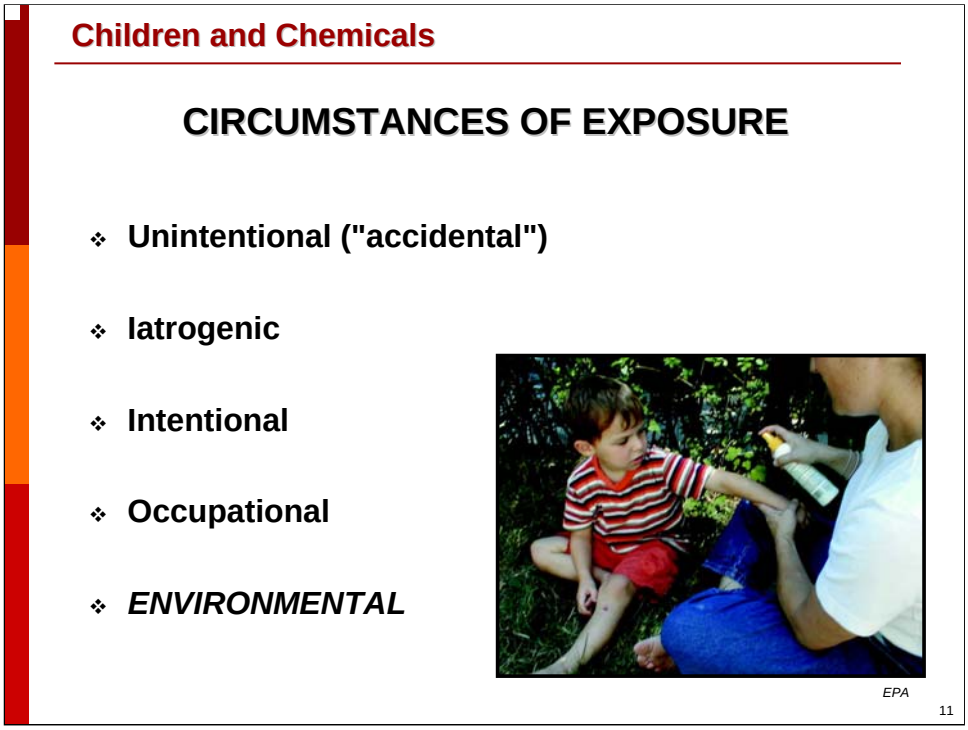
- **Circumstances, sources and type of exposure**
- **Type of chemicals**
- **Media: water, air, soil, objects...**
- **Routes of exposure**
- **Toxicokinetics: absorption, distribution, metabolism, elimination**
- **Toxicodynamics: mechanism of action**
- **Scenarios of different age groups**
- **Clinical and sub-clinical effects**
- **Role of the laboratory ("paraclinical" or laboratory studies)**
- **Treatment**
- **Prevention**

The slide summarizes the main points to address when considering children's exposure to chemicals.

It may be applied when dealing with chemicals on a one-by-one basis (such as lead, mercury, solvent or pesticides), but this presentation will provide a general overview on how, when and where children are exposed to toxicants, their potential effects and the possible solutions.

<<READ SLIDE >>

<<NOTE TO USER: you may not need to read this slide, but let the audience see it – as each point will be addressed in the following slides >>



<< NOTE TO USER: for each circumstance of exposure mention the examples that are pertinent to the area and/or your personal experience>>

The potential circumstances of exposure to chemicals in children are listed here.

•UNINTENTIONAL – also called "accidental" (although this term should be avoided to reduce the implication of "inevitability“) – is the most common circumstance of exposure in small children, who are "little explorers", naturally curious, ready to touch and taste everything at their "ground-level" microenvironment (e.g. colourful pills, berries and plastic bottles).

•IATROGENIC – observed mainly in the medical setting, when medications are wrongly administered (e.g. overdose or medication error).

•INTENTIONAL – although infrequent in children, this may occur in socially poor environments, when children are in the care of psychologically unstable people or living under circumstances of social unrest. These intentional exposures include:

– homicide – e.g. children overdosed with pharmaceuticals, intentionally exposed to carbon monoxide or administered toxicants;

– Munchausen syndrome – simulation or induction of disease in children, in this case through the administration of pharmaceuticals or chemicals, usually by psychologically disturbed individuals close to the child (e.g. mother or caregivers);

– “Chemical” battering – a form of child abuse, through the administration of pharmaceuticals and other substances (e.g. sedatives, sleeping pills, table salt or others);

– Solvent abuse (“sniffing”) – a form of recreational drug use and abuse, seen in older children and adolescents;

– Suicide attempt or "gesture" – real or attempted suicides, observed mainly in young, psychologically unstable adolescents;

– Abortifacient – use of abortion-inducing substances by female adolescents frightened by the consequences of unwanted preganancy; and

– Warfare agents – exposure of children to chemicals used in the context of war (e.g. the Kurd population in Hallajba, Iraq, exposed to mustard gas).

•OCCUPATIONAL – young workers being exposed to dangerous and/or unsafely used chemicals in the workplace, and when engaged in child labour.

•ENVIRONMENTAL – a growing cause of concern and relatively "new" approach to children's health, which has gained due recognition in recent decades. It refers to the exposure of children to chemicals present as pollutants or contaminants in their environment. These chemicals may be from anthropogenic or natural sources. Exposure to high levels may lead to poisoning or to effects that are clinically evident. Chronic exposures to low levels of chemicals are difficult to detect and assess, and may be linked to a large number of health and developmental effects (addressed later in this presentation).

Picture: EPA, "Applying insect repellent"

Children and Chemicals

SOURCES OF EXPOSURE IN THE ENVIRONMENT

- **Anthropogenic "man-made"**
  - **Traffic**
  - **Industry**
  - **Additives and contaminants**
- **Natural**
  - **Arsenic**
  - **Fluoride**
  - **Blue-green algae**
  - **Aflatoxins**

WHO

Ceppi, Corra

<< NOTE TO USER: for each source of exposure mention examples that are pertinent to the area and/or your personal experience on the subject.>>

Anthropogenic sources are those of human origin ("man-made") or industrial. These include the pollution of the environment due to traffic and pesticide residues in food.

As illustrated very graphically in the drawing at the top of the slide made by a schoolchild in India, in preparation for World Health Day 2002, where clouds of air pollutants appear with a "devilish" face….

Natural chemicals are naturally present in the environment, but at levels high enough to cause adverse effects in humans. Typical examples are the elements:

– arsenic in water causes arsenicosis;

– fluoride in water causes fluorosis and fluoride also occurs in the air (produced from the burning of Fl-rich coal);

Other chemicals of natural origin include:

– blue-green algae toxins in recreational waters; and

– aflatoxins in food (a type of mycotoxin which may contaminate maize and other stored grains) has toxic effects on the liver, immune system and other organs, affecting especially children. It represents a public health problem in many African countries.

– cyanogenic glycosides in some foodstuff (e.g. cassava).

Pictures: Up: WHO, C. Gaggero. Environmental water, Americas.

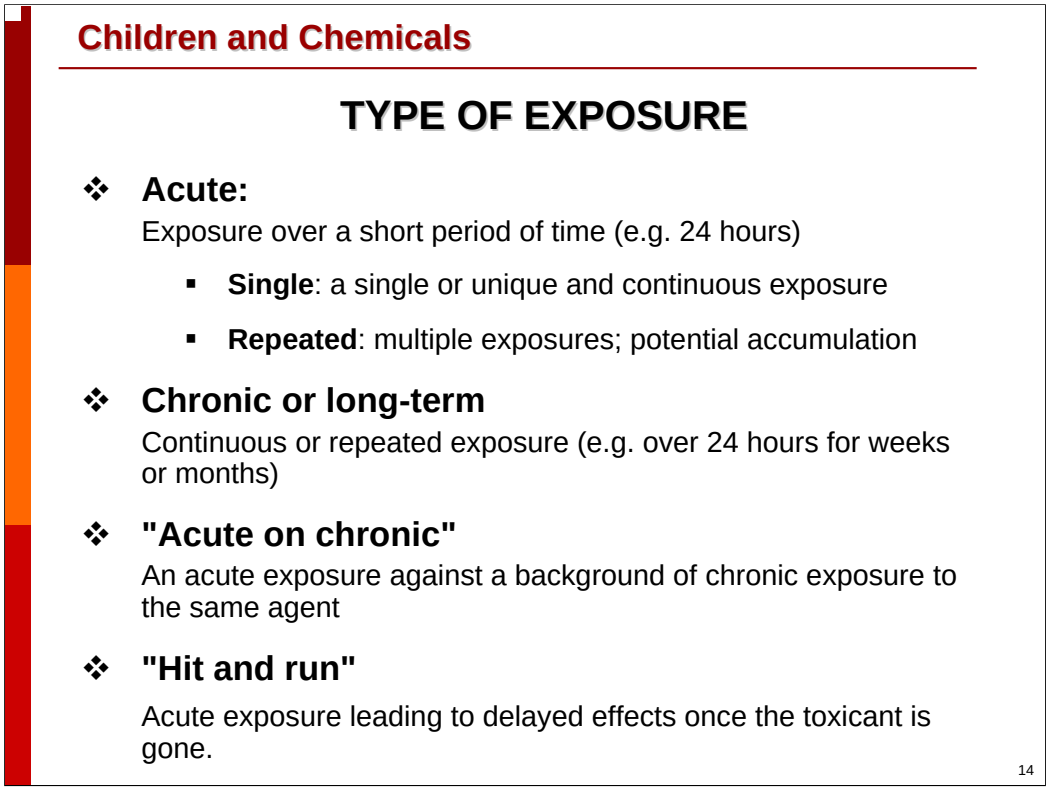
Below: Ceppi, Corra, Argentina. Used with permission.

TYPES OF EXPOSURE

- Acute or chronic
- Acute "on chronic"
- "Hit and run"
- High or low dose
- During "critical" periods

<<NOTE TO USER: These will be explained in the following slides>>

Effects suffered – or not – depend upon the type of exposure, dose and opportunity (timing) as well as on the characteristics of the chemical involved and the clinical, nutritional and developmental status of the child.



<< NOTE TO USER: for each type of exposure, mention the examples that are pertinent to the area and/or your personal experience on the subject.>>

Acute poisonings

Acute poisonings result from exposure to an agent over a short period of time e.g. 24 hours. Acute poisonings may be:

Single: a single or continuous exposure to an agent over a short period of time e.g. for 24 hours (e.g. carbon monoxide).

Repeated: multiple exposures to an agent over a short period of time e.g. 24 hours, where there may be accumulation (e.g. aspirin overdose).

Chronic exposures

Chronic exposures are continuous or repeated exposures e.g. for more than 24 hours, for weeks or months, as is the case of lead poisoning.

"Acute on chronic"

“Acute on chronic” is an acute exposure against a background of chronic exposure to the same agent (e.g. organophosphorus pesticide exposure on a chronically exposed child.

"Hit and run"

Acute exposure leading to delayed effects once the toxicant is gone (e.g. thalidomide exposure during gestation leading to phocomelia).

Ref:

•*PCS, Authority Lists and Definitions for the INTOX Data Management System,*

ACUTE POISONINGS

According to Poisons Centres

- Up to 50% to 70% of the calls are about children exposed to chemicals or actually poisoned
- The majority are between 1 and 4 years old
- Mainly in boys!
- Cases of exposure are mostly acute and accidental
- The outcome is usually favourable
- Mortality is low

However…

<<READ SLIDE>>

<< NOTE TO USER: insert data and statistics provided by the local poisons control centre.>>

Ref:

•*www.who.int/ipcs/poisons/centre/directory/en/*

CHEMICALS – *ACUTE* POISONINGS

❖ **Pharmaceuticals:**	**sedatives, disinfectants, analgesics, contraceptives, syrups, contaminants**
❖ **Household products:**	**bleaches, cleaners, detergents, solvents, kerosene**
❖ **Cosmetics:**	**perfumes, shampoo, nail products**
❖ **Plants and mushrooms:**	**berries, seeds, leaves**
❖ **Drugs of abuse:**	**alcohol, tobacco, illicit drugs of abuse**
❖ **Pesticides:**	**insecticides, rodenticides, herbicides**
❖ **Bites and stings:**	**Snake, scorpions, bees,… "envenomings"**

<< NOTE TO USER: for each type of chemical mentioned, give examples of acute poisons, pertinent to the area and/or your personal experience on the subject.>>

This list includes the types of chemicals most commonly involved in acute childhood poisonings – those that are the most accessible to children in the home and its surroundings.

<<READ SLIDE>>

Ref:

•*Goldfrank, Goldfrank's toxicologic emergencies, Appleton and Lange, 6th edition, 1998.*

HIGH AND LOW DOSE EXPOSURES

- **High- level exposure → poisoning**
- **Low-level exposure → subtle effects**

Great concern raised by persistent organic pollutants (POPs) and potential developmental neurobehavioral and endocrine effects

Effects depend on the type of chemical, the dose and timing of exposure (examples will be presented in future slides)

In general:

•High-level exposures tend to produce poisoning and the diagnosis is usually quite clear. E.g.: child is found with an empty bottle of medicine and presents drowsiness.

•Low-level exposures may produce undetected or subtle effects, which may be of difficult diagnosis. E.g.: lead exposure and anaemia.

TYPE OF CHEMICALS – *CHRONIC* EXPOSURE

- **Metals**
  - **Lead**
  - **Mercury**
  - **PCS**
- **Pesticides in food or fields**
- **Persistent organic pollutants (POPs)**

<< NOTE TO USER: for each type of chemical mentioned, describe examples of chronic exposure that are pertinent to the area and/or your personal experience on the subject.>>

Although any chemical can cause acute toxic exposure, in some instances, low-level, chronic exposures are a cause of concern.

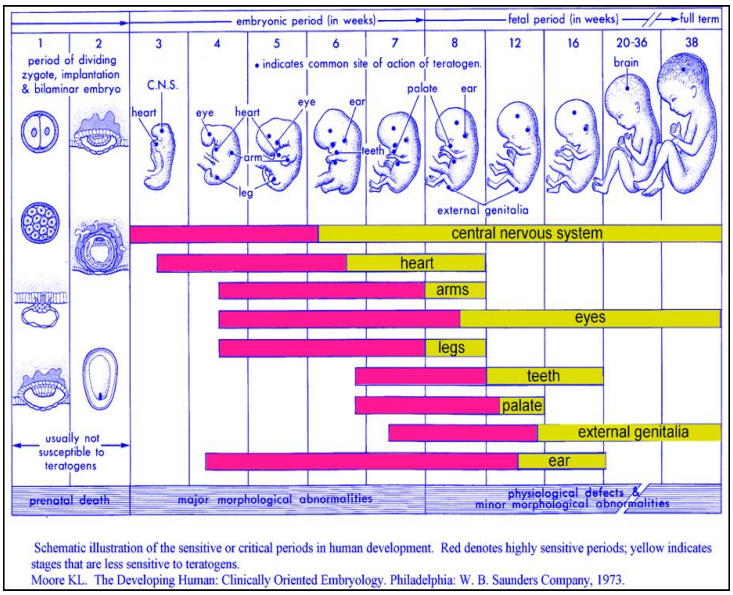
The list includes the types of chemicals involved in chronic, high-level and low-level exposures for which important adverse effects in children have been demonstrated and/or that represent a potential threat (e.g. POPs) are potentially…

<<READ SLIDE>>

Children and Chemicals

DYNAMIC DEVELOPMENTAL PHYSIOLOGY

WINDOWS OF DEVELOPMENT



Schematic illustration of the sensitive or critical periods in human development. Red denotes highly sensitive periods; yellow indicates stages that are less sensitive to teratogens.
Moore KL. The Developing Human: Clinically Oriented Embryology. Philadelphia: W. B. Saunders Company, 1973.

Moore, Elsevier Inc, 1973

Physiological differences manifest in more ways than immature metabolic pathways. Because important systems are still differentiating and growing, children have unique susceptibilities compared to adults — and critical time windows in those susceptibilities.

- •Preconception
- •Gestation
  - – thalidomide, DES
  - – ionizing radiation
  - – methylmercury, Pb
- •Postnatal
  - – second-hand tobacco smoke
  - – lead.

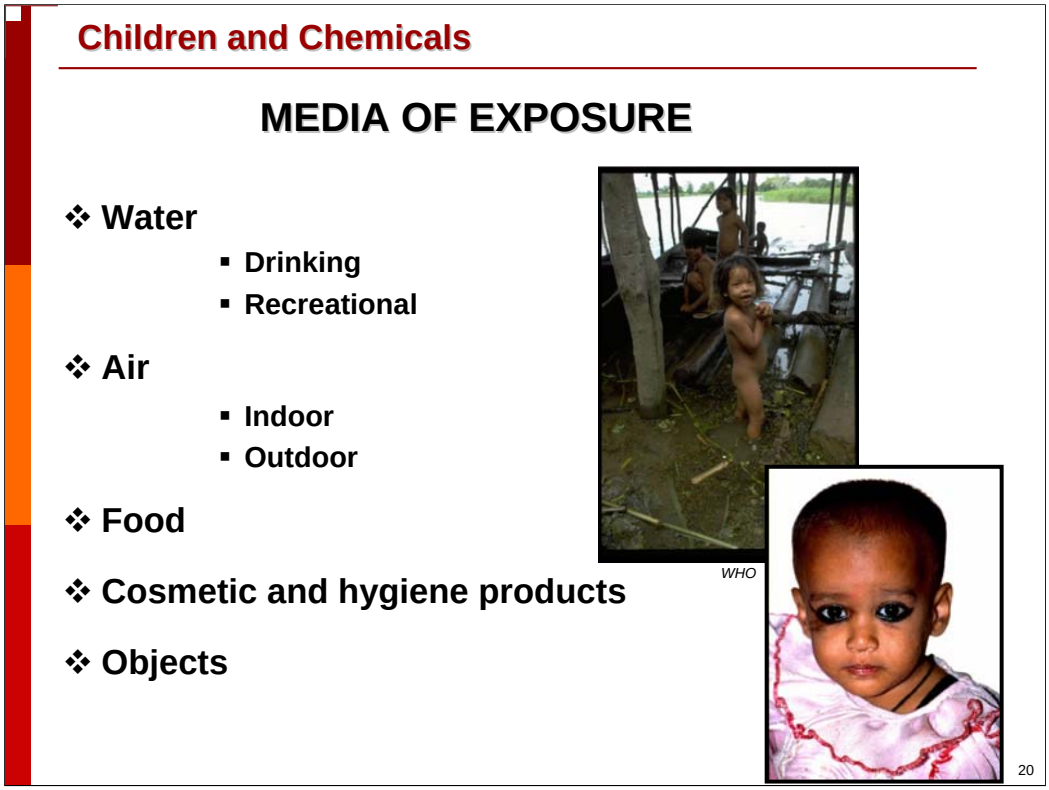
There has been an explosion of knowledge about development in past decade or so, and it is hard to remember that it was only about 50 years ago that the discovery was made that the fetus is vulnerable to exposures. The phocomelia epidemic resulting from use of thalidomide in pregnancy was an early and dramatic example of the ability of chemicals to cross the placenta and damage the fetus. Additionally, thalidomide administered during a small, 4-day window between gestational days 20 and 24, may increase the risk of autism *(Stromland, 1994).* More than one system can be susceptible and different pathology may occur depending upon the dose and timing of exposure.

Now we know that other exposures during gestation can harm systems, and some are listed here. We also know that preconception exposure of both parents can cause harm to children, as well as postnatal exposures.

<<NOTES TO USER: It is important to point out the different responses to insults shown on the bottom bar of the figure. Significant insult during the embryonic phase will result in pregnancy loss (first 2 weeks) or major organ malformation. During the fetal stage, damage is more subtle and related to system dysfunction.>>

Ref: Stromland, Autism in thalidomide embryopathy: a population study, Developmental Medicine & Child Neurology (1994) 36(4):351.
Of a population of 100 Swedish thalidomide embryopathy cases, at least four met full criteria for DSM-III-R autistic disorder and ICD-10 childhood autism. Thalidomide embryopathy of the kind encountered in these cases affects fetal development early in pregnancy, probably on days 20 to 24 after conception. It is argued that the possible association of thalidomide embryopathy with autism may shed some light on the issue of which neural circuitries may be involved in autism pathogenesis.

Figure: Reprinted from The developing human, Moore, Elsevier Inc., 1973. Used with copyright permission (2004) from Elsevier.



<< NOTE TO USER: for each medium of exposure, mention the examples that are pertinent to the area and/or your personal experience on the subject.>>

•*Water*: Used for drinking, cooking, preparation of infant formula, bathing and swimming. Groundwater or surface water may be contaminated by "point" sources of pollution (e.g. industrial discharge) or "non-point" sources such as agricultural and rural run-off, soil contamination and atmospheric deposition. Some contaminants of concern are: arsenic, chromium, lead, mercury, nitrates, benzenes, pesticides, PCBs and disinfectants (such as chloramine and chlorine).

The photo illustrates a situation commonly seen in poor areas, where children play and spend time in contact with unsafe water.

•*Air*: It is important to differentiate between indoor and outdoor pollutants. Indoor pollutants include particulate matter, gases, vapours, (also biological material and fibres). These contaminants are produced by tobacco smoke, stoves and construction materials. Pesticides and other chemicals for household use are present in the home. Outdoor pollutants vary according to density of traffic, extent of industrialization, time (of the year and of the day) and climate. The six main outdoor pollutants are: ozone (O_3), particulate matter (PM_{10} and $PM_{2.5}$), lead, sulfur dioxide (SO_2), carbon monoxide (CO) and nitrogen oxide (NO_2).

•*Food*: Food may have a large range of contaminants: from additives (colourings, flavourings and preservatives) to pesticides (as residues or as contaminants) and mycotoxins, as well as natural toxins in doses high enough to produce toxic effects (as is the case of some shellfish and fish toxins). A major cause for concern has been raised by mercury and PCB contamination of fish and also by the presence of mycotoxins in contaminated grains. Special attention should be paid to the diet of infants, children and adolescents in order to assess potential exposure to toxicants.

•*Cosmetic and hygiene products*: a number of products applied to children may have contaminants with toxic effects (e.g. talcum powder and body lotions.)

The photo illustrates a little girl with "surma" or kohl applied to her eyes – in some instances "surma" may be contaminated with lead.

•*Objects*: toys, baby's cots and other materials that come into close contact with children may have toxic components or contaminants, as was the case for leaded paint used on wooden toys. In the medical domain, great concern exists about the presence of phthalates in tubes and in catheters, as well as in pacifiers. These products may also be found in toys.

Ref: American Academy of Pediatrics, Pediatric Environmental Health, 2nd Ed. Ed: Etzel, AAP

ROUTES OF EXPOSURE

- **Unique exposure pathways**
  - Transplacental
  - Breastfeeding
- **Exploratory behaviours leading to exposure**
  - Hand-to-mouth, object-to-mouth
  - Non-nutritive ingestion
- **Stature and living zones, microenvironments**
  - Surface area to volume ratio
- **Children do not understand danger**
  - Pre-ambulatory
  - Adolescents have “high risk” behaviours

Children have unique exposure pathways. They can be exposed in utero to toxic environmental agents which cross the placenta. Such exposures can be chemical (to pollutants and pharmaceuticals), physical (to radiation and heat) and biological (to viruses and parasites). They can also be exposed to pollutants that pass into their mother’s milk. Neither of these routes of exposure occurs in adults or older children: they are unique to infants.

Children also have pathways that are different from adults due to their size and developmental stage. For example, young children engage in normal exploratory behaviours including hand-to-mouth, object-to-mouth behaviours, and non-nutritive ingestion which may dramatically increase exposure of children compared to that of adults.

Their physical differences also cause them to reside in a different location in the world; they are closer to the ground so heavy pollutants such as mercury will concentrate in their breathing zone and deliberate applications of pesticides and cleaning solutions makes them more readily accessible to small children. Because they are small, they have a high surface area to volume ratio and can have dramatically increased absorption through dermal contact when compared with that of adults.

Children have much more limited ability to understand and move out of danger, both from toxic agents and dangerous situations which could result in injury. This characteristic is obvious in the pre-ambulatory phase, but persists through exploratory toddler behaviour and into the high-risk behaviours seen in adolescence.

Children and Chemicals

TOXICOKINETICS

How are xenobiotics handled by an immature, anabolic body?

- **Energy, water, oxygen consumption**
- **Absorption**
- **Biotransformation**
  - Activation/detoxification
- **Distribution**
  - Fat: water
  - Blood–brain barrier
- **Elimination**
- **Critical windows of development**

WHO

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Toxicokinetics is the term given to all the processes and pathways that a substance goes through in the body (e.g. absorption, transportation, conversion or metabolism and elimination).

Children have a dynamic physiology that is turned up to “high” because of growth demands. In addition, they are vulnerable to damage during the differentiation and maturation of organs and systems.

Xenobiotics or “chemicals foreign to the biological system” utilize metabolic pathways intended for processing of nutrients and for eliminating metabolites. Some xenobiotics are dangerous as ingested and need to be detoxified by metabolism. Others are not dangerous when ingested but may become dangerous when metabolized (for example: paracetamol overdose, methyl alcohol).

Children are in an "anabolic" state and require larger amounts of energy, water oxygen and nutrients than do adults.

Absorption is different and frequently increased in children because they are anabolic and active. They are geared to absorb nutrients very efficiently. E.g.: lead follows calcium which is essential for skeletal and cellular growth. A toddler will absorb between 40 and 70% of a given ingested dose of lead wherease a non-pregnant adult will absorb from 5–20%. Nutritional deficiencies, particularly anaemia which is common in rapidly growing children, will increase lead absorption.

Some xenobiotics are dangerous as ingested and need to be detoxified by metabolism. Others are not dangerous when ingested but become dangerous when metabolized. Either way, these processes are likely to be different in children, but unfortunately not in predictable ways. Particularly during fetal growth and in the first 6–12 months of life, important metabolic pathways such as cytochrome P450 systems and glutathione conjugation are significantly reduced in efficiency. Most known toxicants are detoxified in the body, so immaturity of these systems increases the duration and amount of any given internal dose.

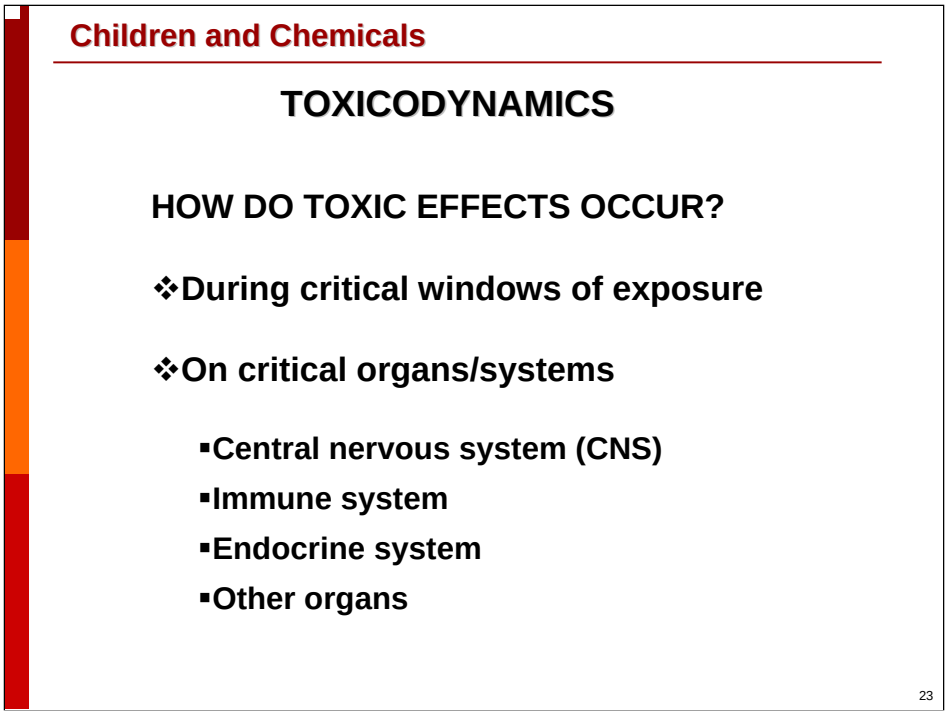
Distribution is different from that in adults and varies with age. For example, the blood–brain barrier is not fully developed for the first 36 months of life; therefore, substances such as lead readily cross into the central nervous system.

Elimination may be decreased in early postnatal life. For example the glomerular filtration rate of a newborn is less that 40% of that of an adult; premature infants may have only 5% of the adult GFR.

All of these physiological processes are likely to be different in children from those in adults, but unfortunately not in predictable ways.

Finally, children’s systems continue to grow, mature and change through adolescence. If disruption occurs during critical periods, the damage may be severe and lifelong. Environmental hazards may harm a developmentally dynamic child by mechanisms that do not operate in the adult.

Ref: Ellenhorn MJ, Barceloux DG. Medical toxicology: diagnosis and treatment of poisoning. Elsevier,



Toxicodynamics refers to the process of interaction between a substance and the organs or systems in the body, resulting in effects. It is equivalent to the "mechanism of action", "toxicity", or "toxic effects".

Effects may occur during:

•*Critical windows of exposure*: every organ develops according to a strict "timetable" in which changes take place at specific times. There are periods during which an organ may be particularly sensitive to the adverse effect of a chemical, radiations or thermal conditions. These are called "critical windows of exposure". For example, in animal experiments, exposure to carcinogenic substances early in life is more likely to trigger cancer than a similar exposure during adulthood. (*Ref: Risk Assessment Forum: Supplemental guidance for assessing cancer susceptibility from early-life exposure to carcinogens. Washington DC, USEPA, Feb. 2003: www.epa.gov/ncea/raf/cancer2003.htm*)

The key target organs in children are the central nervous system (CNS) and the immune and endocrine systems.

•*CNS*: this is a very precisely regulated system that entails numerous processes. Cells divide, multiply, migrate and differentiate; cell connections are continually formed and "pruned"; numerous biochemical changes take place; a variety of neurotransmitters, synapses and receptors are set up to enable the effective transmission of signals. The "brain growth spurt" (period of rapid development) occurs in the fetus in the third trimester of pregnancy and continues into the first 2 years of life. The developing CNS is a potential target for neurotoxic substances. In addition, the blood–brain barrier and detoxification mechanisms may not represent effective mechanisms of protection against toxicants. Developmental neurotoxicants include lead, mercury and PCBs.

•*Immune system*: the immune system develops from "pluripotent" stem cells that migrate from the circulatory system into lymphoid organs (liver, bone marrow, spleen, lymph glands) and differentiate into a wide variety of cell types. These cells (B- and T-lymphocytes, macrophages and granulocytes) learn to distinguish between "self" and "not self" and provide effective resistance against external agents (pathogens and chemicals) without raising auto-immunity. The human immune system is fully formed but not totally protective at birth. Important developments occur after birth, in the interaction with the environment that leads to acquisition of immunological "memory". Toxicants, such as lead, hexachlorobenzene, TCDDs and PCBs may alter the pluripotent stem cells, the T-lymphocytes, the thymus. E.g.: exposure to hexachlorobenzene has been linked to increased prevalence of middle-ear infection in humans (*Ref: Dewailly, Susceptibility to infections and immune status in Inuit infants exposed to organochlorines. EHP (2000) 108 (3):205*).

•*Hormone-dependent sexual development*: hormones are "signalling" substances that enable molecules, cells, tissues and organs to function in a harmonized manner and interact with the environment. Hormones play a crucial role in gender differentiation. Although gender is determined genetically after fertilization, the gonads remain unchanged until week 6, when male sex hormones cause the embryo to develop as a male (if the male hormone is absent, the embryo develops as a female). Later on, hormones control puberty, ovule maturation, spermatogenesis, gestation, birth and lactation.

•The thyroid produces hormones which are crucial for the correct development of organs, such as the brain and the gonads. Some chemicals have been proved to have an endocrine-disrupting (ED) capacity in wildlife, and the *possibility* of such effects in humans is taken seriously as these effects are biologically plausible. The effects may occur by "mimicry" (behaving like hormones), antagonism (preventing their bonding) or disrupting production, conversion, transportation or excretion of hormones. Effects are not only dose-related but also time-dependent: the

Children and Chemicals

For example,

WHO

- ❖ Day-care centres
- ❖ Schools
  - Children spend hours
  - Close to the ground
  - Touching and tasting
  - Pesticides applied remain in carpets and fabrics.

- ✓ Levels of chlorpyrifos vapours in the child's breathing zone (25 cm) are 94 microg/m^3 and 64 microg/m^3 in the adult's breathing zone (100 cm).
- ✓ Exposure of neonatal rats to chlorpyrifos produced brain cell damage and loss, with resultant abnormalities of synaptic development.

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This slide illustrates how exposure may occur, for example in a toddler, in the special settings of the day-care centre, where carpets and fabrics may have been sprayed with pesticides.

Small children have special susceptibilities to exposure because of their:

❖hand-to-mouth behaviour;

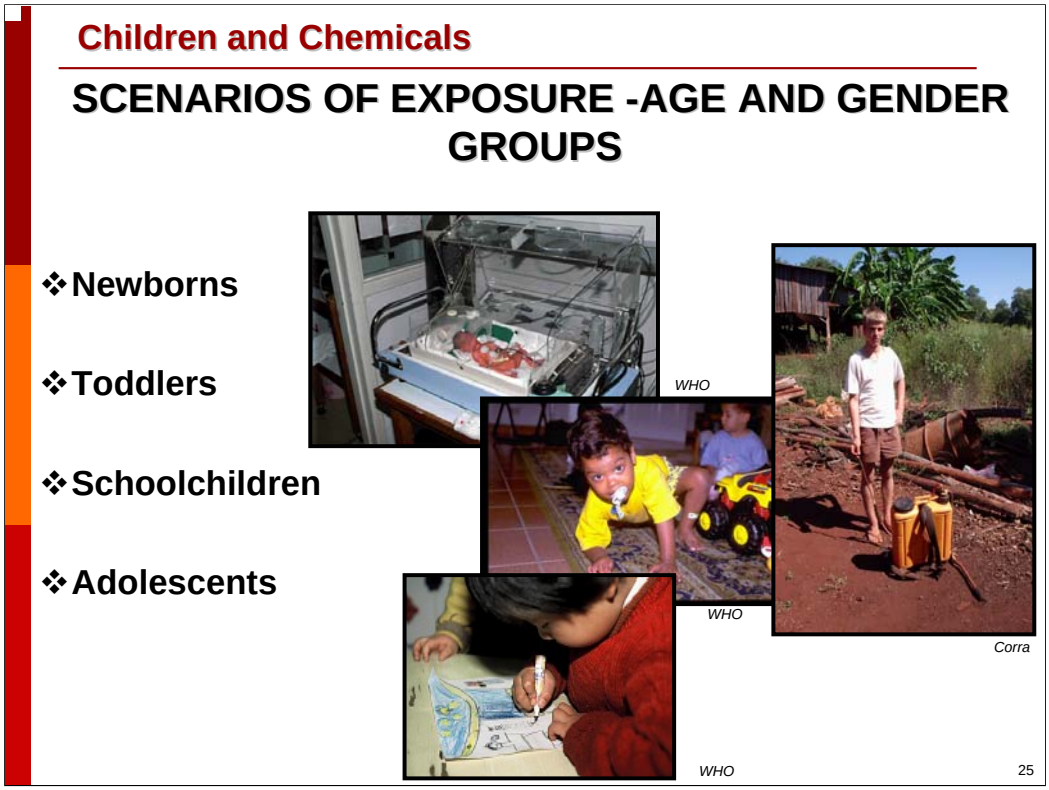
❖ignorance of risks;
❖being close to the ground while playing, crawling or sleeping;
❖behaviour as explorers and investigators (touching and tasting).

Studies on the pesticide chlorpyrifos, an organophosphorus compound which has been used in schools and homes, showed that it has a special volatility and re-evaporation cycle that allows the vapours to concentrate more about 25 cm from the floor (in the child's breathing zone) than in the adult's breathing zone (about 100 cm for a seated adult). The levels of chlorpyrifos measured were 94 microg/m3 in the child's breathing zone and 64 microg/m3 in the adult's breathing zone.

Experiments with neonatal rats showed that chlorpyrifos produced brain cell damage and loss, with resultant abnormalities of synaptic development.

Ref:

•*Qiao, Developmental neurotoxicity of chlorpyrifos: what is the vulnerable period?, Environ Health Perspect. (2002) 110(11):1097*



<< NOTE TO USER: for each scenario, mention the examples that are pertinent to the area and/or your personal experience on the subject.>>

The most common "scenarios" of acute and/or chronic exposure to chemicals for the different age-groups are illustrated in the images presented here.

•*Newborns* – exposure of newborns to chemicals is infrequent, but may occur in a medical setting, when due to medical error or drug contaminants newborns are administered or applied with inappropriate chemicals. As an example, in the nineties, the Swiss daily newspaper *Le Matin*, published details of two lethal cases of poisoning that had occurred in a Belgian hospital as a result of mistaken use of potassium chloride. Two pre-term babies died because they had received potassium chloride that came from wrongly labelled flasks that were supposed to contain a glucose solution. (*Dr. J. Pronczuk, personal communication*).

<< NOTE TO USER: the concern about breast-milk contaminants may be addressed at this point, if relevant. Please make sure that the right message is received by the audience and that the importance of breast-feeding is emphasized. See slides in "Children are not little adults". >>

•*Toddlers* – as they start moving around, exploring, touching and testing, toddlers may come into contact with or ingest cleaners, pesticides and other products unsafely stored in the home and these may be toxic or caustic. One of the main dangers to toddlers is the ingestion of caustic products that may cause permanent damage to the mouth and oesophagus. *Picture: WHO*

•*Schoolchildren* – artwork may expose children to pigments and solvents, and unsafe science laboratory work may expose students to toxic compounds and fumes. School buses may also be a source of exposure to chemicals, as in the case of faulty combustion and carbon monoxide release. *Picture: WHO*

<< NOTE TO USER: consider mentioning the case of Dr Shannon (Boston) regarding schoolchildren exposed to the fumes of school buses whose engines were kept running under the window of a classroom. All children suffered intense headaches and malaise of unknown origin until carbon monoxide was found to be the cause. See Paediatric Environmental History module. >>

•*Adolescents* – one of the typical scenarios is of the young worker who is poorly trained in safe working practices and is exposed to cleaners, pesticides or other chemicals at work. It is also the age when experimentation with drugs may start and youngsters may sniff or inhale solvents, many of which have marked effects on the central nervous system. *Picture: I*

CLINICAL AND SUBCLINICAL EFFECTS

Depend upon:

- **Agent (chemical, physical, biological)**
- **Dose, timing and length of exposure**

May be:

- **Acute and evident**
- **Chronic and subtle**
- **Detected only by laboratory studies**

<< NOTE TO USER: mention clinical examples that are pertinent to the area and/or your personal experience on the subject.>>

The clinical effects observed in children depend upon the type of chemical or pollutant involved, the dose, timing and length of exposure.

Typical examples include:

•Acute poisoning by organophosphorus pesticides, with a characteristic "toxindrome“: miosis, sweating, headache, brachychardia, convulsions.

•Chronic lead exposure: the child may be asymptomatic for some time and then present with anaemia, abdominal pain, fatigue, behavioural changes and learning disabilities.

•Some exposures may not produce obvious clinical effects (e.g. air pollutants, arsenic in water), but will lead to disease after some time or in adulthood. In some instances, these exposures may be assessed through laboratory studies in individuals. Some effects may only be apparent through evaluation of population-wide junction (i.e. IQ testing and population level exposure to PCBs or lead).

ROLE OF THE LABORATORY

- ❖**Confirm exposure to toxicants**
- ❖**Determine its magnitude / severity**
- ❖**Assess and measure effects**
- ❖**Monitor the efficacy of treatment**
- ❖**Follow up the clinical evolution**

Laboratory studies (also called paraclinical studies) are important in the area of paediatric toxicology in order to:

❖confirm exposure (detecting levels in biological fluids);

❖determine the magnitude and severity of exposure;

❖assess and measure effects (e.g. levels of anemia, cholinesterase inhibition, other);

❖monitor the efficacy of treatment;

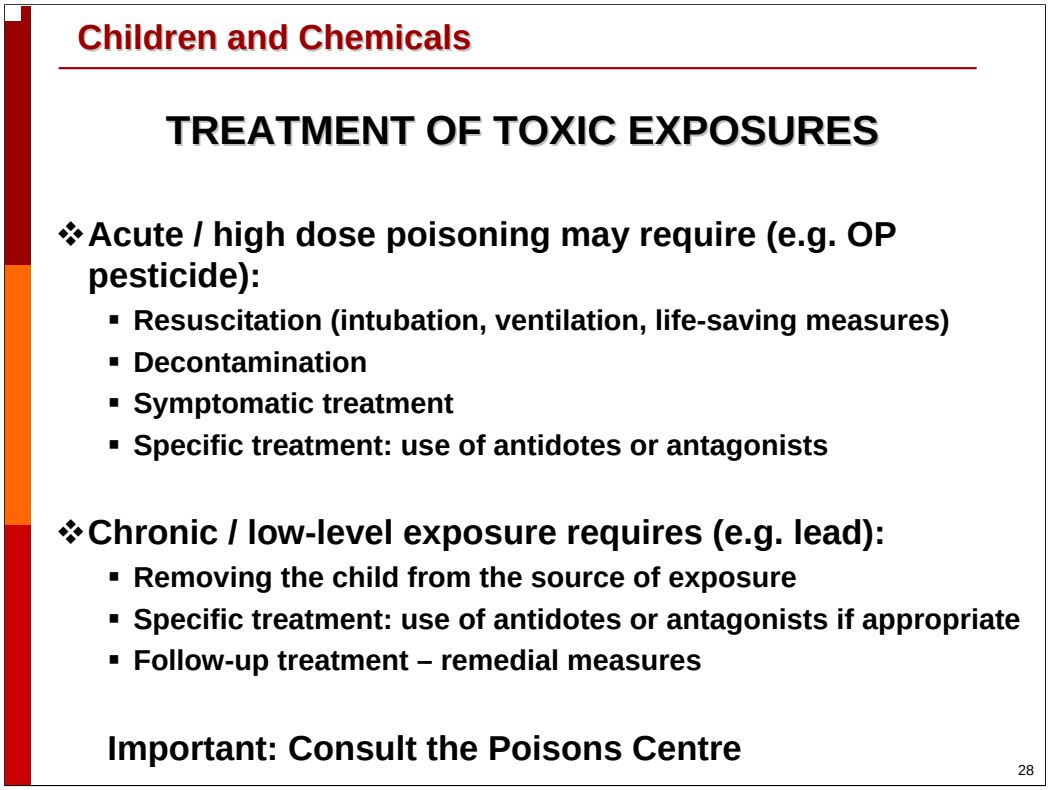
❖follow up the clinical evolution.

<< NOTE TO USER: mention examples that are pertinent to the area and/or your personal experience on the subject.>>

Suggested examples:

-Lead exposure – measuring blood lead levels and using these to assess the need for chelation therapy.

-Exposure to organophosphorus pesticides – confirmation by measurement of cholinesterase in red blood cells or full blood.



The treatment of toxic exposures in children varies according to the chemical involved, the type/level of exposure, the clinical effects observed and also according to the results of laboratory studies.

<< NOTE TO USER: mention one or two examples of acute and chronic exposures to illustrate how treatment differs>>

Specific examples

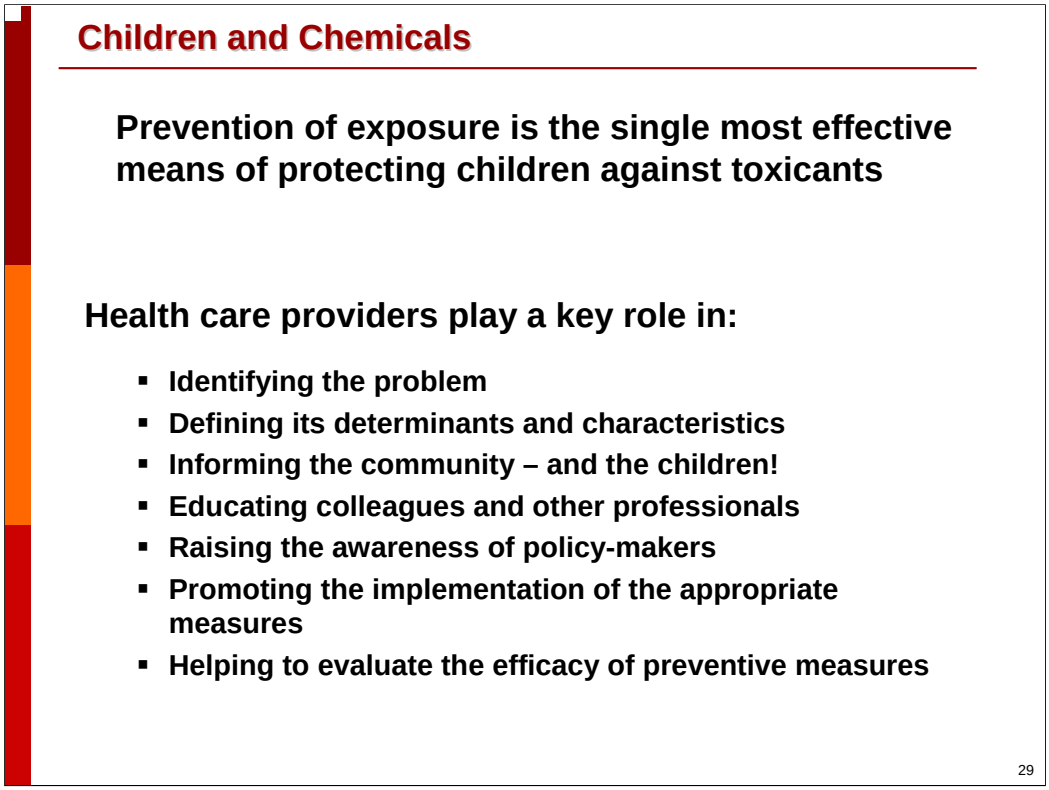
Organophosphorus (OP) pesticide

Acute poisoning by an organophosphorus pesticide may require decontamination (washing of the skin, or possibly gastric lavage, under special circumstances), drying bronchial hyper secretion with atropine and the administration of enzyme reactivators (pralidoximes).

Lead

Chronic lead exposure requires removal of the child from the source of exposure (e.g. contaminated soil or water, paint chips in the home, stopping use of leaded ceramics) and personal and home hygiene measures. Environmentally-exposed children may have a blood lead level of around 10–15 microg/dL. If blood lead levels are above 45 microgram/dL, the use of a chelating agent (succimer) should be considered. If the child presents with lead encephalopathy, intensive care is required as well as the administration of chelating agents (BAL and succimer).

Ref: Winneke, Neurobehavioral aspects of lead neurotoxicity in children, Cent Eur J



<< NOTE TO USER: mention success stories of prevention of toxic exposures and exposure to pollutants. Give examples that are pertinent to the area and/or your personal experience on the subject.>>

Health care providers play a key role in many aspects of the prevention of exposure. These are:

•*Identifying the problem*. What are the main toxic exposures in children? What are the main causes of acute poisonings? Are there any cases of chronic exposure to environmental pollutants? Is there a high incidence of diseases that may be linked to chemicals in the environment? Paediatric emergencies and poisons centres are able to provide statistical and epidemiological data on the subject.

•*What are the determinants and characteristics?* Are exposures in children acute or chronic? Where do they occur? When and how? Are there any predisposing factors? Which populations or groups are affected? Are they predominantly urban or rural?

•*Informing the community – and the children*! The community whose children are exposed to chemicals and pollutants in the environment should be informed about the situation in a clear manner (*do not hide!...do not scare!).* Social workers and communications experts may provide valuable advice on how to communicate risks or potential threats to the community, and how its members may avoid them and protect their children.

•*Educating colleagues and other professionals.* It is especially important to educate those who should recognize and manage the effects of chemicals on children's health (e.g. nurses, physicians, primary health care workers). Those who will help in assessing environmental issues should also be educated.

•*Raising the awareness of policy-makers about the problems identified*. Policy-makers should be made aware of the risks facing children – poisonings and potential chronic exposures.

•*Promoting the implementation of the appropriate actions*. The implementation of the appropriate measures should be promoted in consultation with key partners including policy-makers, doctors, nurses, teachers and parents.

•*Evaluating the efficacy of preventive measures*. The efficacy of preventive measures should be

International agreements on the protection of children's health from the effects of chemicals

- **1992 Agenda 21, Ch. 25 (United Nations Conference on Environment and Development)**
  www.un.org/esa/sustdev/documents/agenda21/index.htm
- **1997 Declaration of the Environment Leaders of the Eight on Children's Environmental Health**
  yosemite.epa.gov/ochp/ochpweb.nsf/content/declara.htm
- **1999 Declaration of the Third European Ministerial Conference on Environment and Health** *www.who.dk/AboutWHO/Policy/20010825_2*
- **2002 Bangkok Statement (WHO International Conference)**
  www..who.int/ceh
- **2003 Recommendations of the Intergovernmental Forum on Chemical Safety (IFCS) on Children and Chemicals** *www.ifcs.ch*
- **2004 Budapest Ministerial Conference on Environment and Health (CEHAPE)** *www.euro.who.int/childhealthenv/Policy/20030625_1*

A number of international recommendations and agreements refer to the protection of children's health from the effects of chemicals.

<<NOTE TO USER: Mention the agreements that are relevant to the setting of the course and participants, and mention those ratified and/or followed-up in the country.>>

WERE THE LEARNING OBJECTIVES REACHED?

- **Learn about chemical hazards in children – what they are and what are the risks they may pose?**
- **Identify the scenarios – how, where and when are children exposed?**
- **Recognize signs, symptoms and diseases that may be related to acute and chronic toxic exposures in children**
- **Know how to assess, prevent and manage children's toxic exposures**

<< NOTE TO USER: go through the learning objectives summarizing what has been presented and checking whether the objectives were accomplished.>>

More information on specific chemicals is available in other modules (e.g.: lead, mercury, pesticides, heavy ,metals, …)

CHILDREN AND TOXICANTS

Carolina

Acute and chronic, high and low-level exposures to chemicals in the environments of children may cause functional and organic damage, during periods of special vulnerability

“Children are not little adults”…

Informed health care providers play a key role in preventing and managing.

<<READ SLIDE>>

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