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

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

This module is based on the WHO module “Pesticides”. First draft prepared by Amalia Laborde MD (Uruguay).
Pesticides and Children

LEARNING OBJECTIVES

- Learn about pesticides – what they are and what are the risks they may pose?
- Identify the scenarios – where and when are children exposed?
- Recognize signs, symptoms and diseases that may be related to pesticide exposure in children
- Know how to prevent and treat children's pesticide exposure

<<READ SLIDE.>>
OVERVIEW

- Origin, environmental transport and fate of pesticides
- Routes and circumstances of exposure
- Toxicokinetics and toxicodynamics
- Target organs and systems
- Diagnosis and treatment of poisoning
- Prevention of pesticide exposure and poisoning
Pesticides have numerous beneficial effects. These include crop protection, preservation of food and materials and prevention of vector-borne diseases.

For example pesticides may be used in the prevention of malaria, which kills up to 1 million children per year, and for preventing other vector-borne diseases such as dengue, leishmaniasis and Japanese encephalitis.

Pesticides are toxic by design – they are BIOCIDES, designed to kill, reduce or repel insects, weeds, rodents, fungi or other organisms that can threaten public health and the economy.

Their mode of action is by targeting systems or enzymes in the pests which may be identical or very similar to systems or enzymes in human beings and therefore, they pose risks to human health and the environment.

Pesticides are ubiquitous in the environment and most are synthetic.

There is growing concern about children's exposure to pesticides and their special susceptibility. Children are not little adults, and may have higher exposures and greater vulnerability at both high and low levels of exposure.

**Ref:**

In the USA, the use of pesticides doubled from 1960 to 1980, but total use has since remained stable or fallen. Most pesticides are used in agriculture, but in 1999 about 74% of households in USA were reported to use at least one pesticide in the home.

Although developing countries use only 25% of the pesticides produced worldwide, they experience 99% of the deaths. This is because use of pesticides tends to be more intense and unsafe, and regulatory, health and education systems are weaker in developing countries.

Pesticides and Children

USE OF PESTICIDES – TYPES OF PRODUCT

- Pesticides used in different settings: Agricultural, Veterinary, Domestic, Institutional

- Formulations: liquid, gel, paste, powder, granules, pellets, baits...

- Concentrations: from 2% to 80% of active ingredient

- Containers: glass, plastic or metal flasks, bottles, drums, plastic bags or paper bags....

<<READ SLIDE.>>

• It is important to consider the presentation, concentration and formulation of the products, as the toxic effects depend on the physical state of the product and also on the characteristics of the solvent or other substances contained in the formulation.

• The rate of absorption depends upon the presentation of the product: volatile pesticides and fine powders are more easily inhaled than dense products and coarse granulated materials.

• Concentrated solutions are much more dangerous than then diluted ones; solid baits may be colourful, attractive and sweet, and may be easily ingested by toddlers.

• In some cases, if the concentration of the active compound is less than 2% (as is generally the case for pesticides for household use) the toxicity in cases of human exposure may be due to the solvent (e.g. kerosene or paraffin) and not to the active ingredient.

Refs:
• IPCS. The WHO Recommended Classification of pesticides by hazard, Guidelines to Classification 2000–2002 (www.inchem.org/documents/pds/pdsother/class.pdf)
There is a large variety of pesticides designed to kill specific pests – those most widely used are listed below.

- **Insecticides** (for killing insects) such as organochlorines, organophosphates and carbamates. This category also includes insect repellents such as diethyltoluamide (DEET) and citronella (of natural origin).

- **Herbicides** or weedkillers (e.g. paraquat, glyphosate and propanil).

- **Fungicides** (to kill mould or fungi): when applied to wood, they are called wood preservatives.

- **Rodenticides** (to kill mice, rats, moles and other rodents).

- **Fumigants** are pesticides that exist as a gas or a vapour at room temperature and may be used as insecticides, fungicides or rodenticides, especially in closed storage places – as they kill every living organism. They are extremely toxic, due to their physical properties, rapid environmental dissemination and human or animal absorption (examples include cyanide, aluminium phosphate and methyl bromide).

- **Other pesticides** include algaecides (to kill algae), miticides (to kill moths) and acaricides (to kill ticks).
There are many groups of chemicals used as pesticides. There are hundreds of different active principles or main ingredients of pesticide groups (e.g. approximately 300 in Uruguay and 900 in the USA).

<<NOTE TO READER: insert the number in your country/region.>>

Some domestic, agricultural or veterinary products may contain more than one chemical belonging to the same or a different chemical group.

Exposure or emission into the environment can occur from on-site exposure through spraying or application of solid formulations to different targets. For example exposure can occur during:

- agricultural use (spraying fields) or seed treatment;
- use in cattle dips and in animal husbandry;
- use as household insecticide (indoor), or in gardens;
- sanitary indoor use in schools, offices, hospitals and other institutions;
- public health use (outdoor or indoor): in parks and urban areas and for vector control (e.g. malaria, Chagas disease, dengue and onchocercasis);
- medical human use: to treat head lice or scabies; and
- veterinary products for pets (e.g. to treat infestations with fleas or ticks).


Pesticides have different distribution and persistence patterns in the environment, even if all of them are distributed in some way through air, soil and water. This should be addressed to gain an understanding of how acute and chronic exposure may occur because air, water and soil are the media of exposure.

This scheme illustrates the routes followed by an agricultural chemical (spray, granulate or seed treatment) that is applied to a given site, representing a risk to applicators, bystanders and wildlife.

When a pesticide is applied directly to a target pest (plant or animal) the whole site is affected including crop plants, soil organisms and, potentially, humans and wildlife in the immediate area. In addition, part of it goes to the air or to surface waters, due to emission (1) or drift (2). Once on the target site, the pesticide may "drain" (6) into surface waters or volatilize (7) into the air. From the air it may deposit (3) on humans, wildlife or plants or on the soil. From the animals or plants where it was applied the pesticide may leak (5) into groundwater.

Pesticides in surface water may go into aquatic organisms, and by sedimentation (4) into other organisms that remain in the sediment.

The persistence of the pesticide depends on its physical and chemical properties (partition coefficients, degradation rates, deposition rates) and the characteristics of the environment. Climate characteristics also play a role in persistence. Studies in the Arctic have shown that insecticides and herbicides persist 3 to 8 times longer in cold climates than in temperate ones.

The most persistent pesticides are termed “persistent organic pollutants” (POPs) and are addressed in a separate module.

Some pesticides are characterized by being very persistent in the environment. They may represent long-term dangers as they biomagnify up the food-chain. Humans, and particularly breastfed babies, are at the top of the food-chain.

• Most POPs (persistent organic pollutants) (these will soon be considered as persistent toxic substances or PTS) are organochlorine pesticides, namely, aldrin, endrin, chlordane, DDT, heptachlor, mirex, toxaphene and hexachlorobenzene.

• They have been banned for agricultural or domestic uses in Europe, North America and many countries of South America in accordance with the Stockholm Convention (ratified in 2004). However, some organochlorine pesticides are still used – e.g. DDT is used to control malaria in some developing countries.

• Other POPS or PTS include industrial chemicals (PCBs, HCB) and unintended byproducts (dibenzo-p-dioxins, dibenzofurans), and other chemicals.

• These persistent chemicals are controlled under the Stockholm Convention.

• They are typically lipophilic compounds that are resistant to environmental breakdown and accumulate in adipose tissue.

• They bio-concentrate in fish, wildlife and human tissues.

• The highest levels are found in marine mammals.

• There is concern about potential endocrine and developmental effects, especially in children.

The US Geological Survey (USGS) monitors ground and surface water for 76 pesticides and seven pesticide breakdown products. A recent survey found that 90% of streams and 50% of wells tested were positive for at least one pesticide.

Ref:
• USGS: ca.water.usgs.gov/pnsp/index.html

In many respects, the greatest potential for adverse effects of pesticides is through contamination of the hydrological system, which supports not only human life, but also aquatic life and related food-chains. Water is one of the primary means by which pesticides are transported from their areas of application to other parts of the environment. Thus, there is potential for movement of pesticides into and through all components of the hydrological cycle (see picture).

Ref:
• USGS: ca.water.usgs.gov/pnsp/atmos/atmos_1.html
Detection frequencies for those pesticides that have been analysed in air and rain at 10 or more sites in the United States.

Ref:
• USGS. Pesticides in the atmosphere: ca.water.usgs.gov/pnsp/atmos/atmos_4.html
Pesticides and Children

CHILDREN'S EXPOSURE

A cause of concern

- Multiple chemicals
- Multiple sources of exposure
- Multiple routes of exposure
- Multiple effects

Pesticides are considered one of the main environmental threats to children’s health because:

• A large variety of chemicals and mixtures are used as pesticides.
• Many pesticides are used at the same time in the same place (agricultural regions).
• They are ubiquitous in the environment – and in individual environments (micro-environments) of children – there may be several sources of exposure to the same or a different chemical.
• Multiple exposures may occur from the preconception period throughout the child's growth into adolescence and adulthood.
Pesticides and Children

CHILDREN’S ENVIRONMENTAL EXPOSURE

- Pesticides used in: homes and schools, playgrounds, parks, fields and other public places
- Children living on: farms, agricultural areas (rural setting)
- Pesticides present in: air, soil, food, water, objects...

Different scenarios:
- ACUTE high-level exposure, overt poisoning
- CHRONIC low-level, chronic exposure, various effects

Children are exposed in different settings and by a variety of routes.

- Pesticides may be unsafely used in the home, by parents who want to protect their children from mosquitoes, cockroaches or rodents. Different pesticides may be stored within the reach of children. They are also used in schools and playgrounds (in treated wood) and in green areas (parks and playing fields) to destroy weeds.

- Living on farms or in agricultural areas, where pesticides are frequently and heavily used, is a high-risk scenario for exposure.

- Pesticides may be present in food and water, either as residues from treatment of crops or at higher levels, as a result of contamination.

- In some areas, there is a potential for release into the environment during production and formulation of pesticides (in factories).

- These are the circumstances under which children may receive acute and high-level exposure leading to poisoning or chronic, low-level exposures linked to more subtle, developmental and other effects.
Pesticides and Children

**SOURCES AND SETTINGS OF EXPOSURE...**

**HOME, SCHOOL, DAY-CARE, INSTITUTIONS...**

*Indoor and outdoor application*
- Mosquito control
- Professional/domestic application
- Lice or scabies
- Fleas or ticks on pets

*Pesticide residues*
- Dust, soil, furniture, carpets, toys, food...
- Playgrounds, playing fields, lawns, gardens
- Wood preservatives in play structures
- Long range transport of POPs (e.g. DDT)

**Pesticide application**
- Professional application of pesticides both indoors and outdoors is used increasingly commonly for the control of rodents, cockroaches, ants, termites, earwigs and other pests. Signs and symptoms of pesticide-related illnesses have been described after indoor and outdoor spraying.
- Domestic use of insecticides is also a source of exposure. Insecticides formulated as sprays, strips and baits are widely available.
- Certain topical pharmaceuticals for direct application on children’s skin or scalp contain insecticides to control lice or scabies. Their use carries a risk of acute (chronic if repeated) overexposure. High doses or applications lasting a long time have caused acute poisoning. There are many pharmaceuticals described in the *International pharmacopoeia* that contain organophosphorus (malathion) and organochlorine (lindane) pesticides still being used to treat head lice. Such products may contain up to 2% of pesticide.
- Dogs and cats are often treated with insecticides to control fleas or ticks. Veterinary products can be as concentrated as agricultural ones. Pet dips for treatment of flea infestations usually contain organophosphate and pyrethroid pesticides. Children are often involved in pet care.

**Pesticide residues**
- Insecticides may persist in house dust, in soil tracked in from outdoors, in carpets, toys, food and furniture.
- High levels of insecticides have been measured for weeks after professional application.
- Residues of organophosphorus insecticides sprayed in indoor environments have been reported to occur on floors, carpets, children’s toys, furniture, bed covers and in dust.
- Poor hygiene habits or houses that are difficult to clean increase the risk of exposure.
- Playgrounds, playing fields, lawns and gardens may be routinely sprayed in order to keep insects away.
- Pesticides are found in recreational waters (lakes, rivers and in pools (algaecides)).
- Persistent wood preservatives such as arsenic/copper/chromium mixtures have been used on play structures.
- The persistent organic pollutants (POPs) include nine pesticides.

- CDC Surveillance for acute insecticide related illness associated with mosquito control efforts Nine States 1999–2002 (www.cdc.gov/mmwr/preview/mmwrhtml/mm5227a1.htm).

Picture: WHO
**Pesticides and Children**

**SOURCES AND SETTINGS OF EXPOSURE**

Children living on farms or in agricultural areas are exposed:

- to pesticide drift from sprayed fields
- to contaminated soil around living areas
- to contaminated equipment and clothes
- when playing around treated fields
- while helping parents with spraying
- … or with dips in animal husbandry
- when working as child labour

The rural setting is of particular importance for children and young adults.

Children may be exposed to pesticide drift from fields that are being sprayed.

Acute “unintentional” poisoning is possible when small children play with pesticide bottles and colourful containers that have been discarded in their playing areas.

Highly concentrated pesticides may be stored in rural homes.

Parents who are farm-workers or applicators may bring pesticides into the home through contaminated clothes, shoes or equipment.

Children may accompany their parents and help them with their tasks.

Infants who are still being breastfed are often carried by their mothers in the fields.

Children may help with agricultural tasks or may be allowed to play around the sprayed field.

Re-entry intervals (the time required before it is safe to return to a treated area) are not always respected or may be established on the basis of criteria that ensure adult safety only.

Concern is increasing about child labour and young workers.

Although few data are available, it is generally assumed that children make up a substantial part of the agricultural workforce in developing countries. They could be at a higher risk because they are less experienced and assertive than adults; they may lack protective equipment and receive less training or none at all.


*Picture: L. Corra. Child working with pesticides, Argentina. Used with permission.*
Pesticides and Children

Increase in the levels of organophosphorus (OP) metabolites (DAP) paralleling pesticide spraying in a rural area

Koch EHP, 2002, 110 (8): 829

Numerous studies on children's exposure have demonstrated the absorption of pesticides. Pesticide metabolites are used as biomarkers of exposure, and children often have higher levels than adults. Younger children may have higher levels than older ones.

Levels of pesticides were associated with residence in rural areas AND with domestic use of pesticides. The figure shows levels of dialkylphosphates (DAP) in children living in agricultural areas. Levels were measured in many samples taken over 1 year and were found to increase in parallel with periods of pesticide application.


We measured organophosphorus (OP) pesticide exposures of young children living in an agricultural community over an entire year and evaluated the impact of agricultural spraying on exposure. We also examined the roles of age, sex, parental occupation, and residential proximity to fields. We recruited 44 children (2–5 years old) through a Women, Infants, and Children clinic. We collected urine samples on a biweekly basis over a 21-month period. Each child provided at least 16 urine samples, and most provided 26. We analysed samples for the dialkylyphosphate (DAP) metabolites common to the OP pesticides. DAP concentrations were elevated in months when OP pesticides were sprayed in the region's orchards. The geometric means of dimethyl and diethyl DAPs during spray months were higher than those during nonspray months (p = 0.009 for dimethyl; p = 0.018 for diethyl). Dimethyl DAP geometric means were 0.1 and 0.07 micro mol/L for spray months and nonspray months, respectively (57% difference); diethyl DAP geometric means were 0.49 and 0.35, respectively (40% difference). We also observed differences for sex of the child, with male levels higher than female levels (p = 0.005 for dimethyl; p = 0.046 for diethyl). We observed no differences due to age, parental occupation, or residential proximity to fields. This study reports for the first time the temporal pattern of pesticide exposures over the course of a full year and indicates that pesticide spraying in an agricultural region can increase children's exposure in the absence of parental work contact with pesticides or residential proximity to pesticide-treated farmland.


Figure: ehp.niehs.nih.gov/members/2002/110p829-833koch/koch-full.html
Reproduced with permission from Environmental Health Perspectives
Some pesticides are volatile and can be inhaled over a period of hours or days because of the volatilization from contaminated surfaces. Particulate material under 10 microns is breathable, and the smaller particles are more dangerous because they can reach the alveoli. Children can be exposed when they are around the spraying area.

The persistence of pesticides in the soil depends on their chemical characteristics and many pesticides used in homes have been found, many days to weeks after the application, in house dust. The behaviour of children (e.g. crawling and hand-to-mouth) facilitates exposure.
Once used or spilled, pesticides may contaminate the water used for drinking or bathing. Pesticides can contaminate nearby groundwater and surface water. There is increasing concern about dietary ingestion of pesticide residues by children, in both plant and animal products. The Oregon Child Development Coalition (OCDC) is completing a series of tests to measure the effects of second-hand pesticide exposure in the young children of migrant farm workers. The study was designed to show whether chronic low-dose exposure to pesticides could be causing health and developmental problems in these children.

Details are available at: www.ohsu.edu/croet/aghealth/family.html

<<READ SLIDE.>>
PESTICIDES IN DIFFERENT MEDIA

Food residues

- Many food products have detectable levels of pesticides
- Guideline levels of pesticides in food (MRL)
- Guidelines to limit the population exposure (ADI)
  - Acceptable daily intake (ADI)
  - Increasing concern about cumulative dietary exposure

All industrialized countries have food monitoring programmes that measure pesticide residues. Levels exceeding the maximum established limits have been reported occasionally in monitored food.

Maximum limits for residues have been established only for certain pesticides. Although a single pesticide may be considered safe at a particular level, foods may contain residues of several pesticides at the same time (see the next slide for an example of the pesticide application scheme in apple trees).

Locally grown food may not be properly monitored or controlled for residues of pesticides. Families who eat food directly brought in from fields may have higher pesticide exposure.

A study of cumulative dietary pesticide intake in children from an agricultural community showed that up to 56% of the children exceeded the acceptable chronic dietary doses (Fenske, 2000).

Refs:
- www.who.int/ipcs/food/jmpr/en/
- www.codexalimentarius.net/
- www.who.int/water_sanitation_health/dwq/guidelines/en/

Picture: WHO (L. Taylor), Nutrition, 1994
EXAMPLE OF SEASONAL PESTICIDE USE

APPLE ORCHARD CALENDAR

AUTUMN
- Herbicides: simazine, paraquat, 2-4D

WINTER
- Fungicides: dinitroorthocresol (DNOC)
- Insecticides: organophosphates

SPRING
- Fungicides: Cu salts, dithiocarbamates
- Insecticides: endosulfan, OPs

SUMMER
- Insecticides: OPs

Ref: Dr A. Laborde, Uruguay

<<NOTE TO USER: Include your local calendar for pesticide treatment of APPLES or any other agricultural tasks.>>
<<NOTE TO USER: How many pesticides may be found in an apple? Will "Snow-White" be offered a poisoned apple?>>

More than 10 different chemicals may be sprayed on apple trees or other vegetable crops before harvest.

The example of a calendar of pesticide application in apple trees in Uruguay was provided by Dr A. Laborde.

Ref:

TOXICOKINETICS

❖ Absorption
  ▪ Dermal, ocular, ingestion, inhalation, injection

❖ Distribution and storage
  ▪ Fat soluble pesticides are stored in adipose tissue

❖ Biotransformation
  ▪ Into inactive or more active metabolites

❖ Elimination
  ▪ Urinary excretion
  ▪ Biliary / faecal excretion
  ▪ Excretion in milk

Toxicokinetics depend on the specific pesticide and its chemical properties. Routes of absorption are explained in the following slides.

• The biotransformation of most pesticides involves a combination of several chemical reactions including oxidation, reduction, hydrolysis and/or conjugation, producing different metabolites that may be more or less active (toxic).

• Biotransformation of some organophosphate pesticides involves oxidative activation (e.g. parathion = paraoxon).

• Pesticides may reach different organs and tissues. Many pesticides accumulate in the adipose tissues.

• Elimination is urinary, biliary and faecal.

• Excretion in milk has been experimentally found to be proportional to blood dosage for DDT, dieldrin, aldrin, heptachlor and other organochlorine pesticides.

Ref:

Almost all pesticides are absorbed by these routes.

Different routes are associated with different settings and media of exposure. However, there are settings in which more than one route of exposure can occur (e.g. in an occupational setting).

Pesticides can cross the epithelium of the skin and mucous membranes that exchange gases (alveoli) or nutrients (gastrointestinal mucosa).

The rate of absorption depends on the chemical properties, amount of the chemical, length of exposure and the physical state of the molecule. There are also other factors that may contribute to increased absorption. Skin absorption is higher when there is vasodilatation (e.g. in summer, or with heating). Respiratory absorption is many times higher when respiration is more rapid (e.g. when playing or running). (Transplacental exposure is considered in the next slide.)

In relation to their body weight, children have a larger skin area than adults, breathe in more air and drink and eat more. These aspects and certain childhood behaviours such as putting fingers and objects in their mouths allow exposure to larger amounts of pesticide per kilogram of body weight.

Pesticides can cross the placenta:
• They have been detected in the amniotic fluid and body tissues of human fetuses even during early stages of prenatal life.
• Pesticides have also been found in the meconium.
• Measuring organophosphate (OP) metabolites in meconium is considered a good biomarker of prenatal exposure because meconium starts to accumulate in the 16th week of pregnancy and is eliminated following delivery.

Breast milk may be contaminated and represents the very top of the food-chain:
• Residues of organochlorine pesticides and POPs have been detected in breast milk (including DDT, HCB and HCH isomers) in contaminated areas.
(This issue is considered in the module on Children and Chemicals.)

Refs:

*Picture: WHO, P. Virot. Portrait of a young baby breastfeeding, Delhi, India, Asia, November 2002.*
Pesticides and Children

METABOLIC PATHWAYS

- Organophosphates metabolize into:
  - Oxones
  - Specific inactive metabolites (ME)
  - Non-specific metabolites: dialkylphosphates (DAPs)

Metabolism may either activate or inactivate the chemical. Therefore, immature metabolic pathways may be protective or increase the danger from specific chemicals.

As an example, organophosphates are metabolized to oxones (active metabolite), but also to other specific inactive metabolites (ME) and to non-specific metabolites (the dialkylphosphates (DAPs)) (shown in the figure).

DAPs are used as biomarkers of environmental exposure to all kinds of organophosphate pesticides because DAPs are metabolites of all these pesticides.

Ref:


Figure: Reproduced with permission from *Environmental Health Perspectives*
Several mechanisms of toxicity have been described and these differ according to the specific properties of the pesticide. They are summarized below.

- Irritation is a local effect due to contact of the pesticide with the skin, eyes or other mucosa.
  - The effects are usually redness and pain.
  - Respiratory irritation can produce nasal, laryngeal or pulmonary effects.
  - Most herbicides and fungicides are strong irritants.
- Allergic sensitization is a common effect of pesticides, especially fungicides.
- Enzyme inhibition (e.g. cholinesterase activity is decreased by exposure to organophosphates).
- Oxidative damage (e.g. paraquat is a promoter of superoxide radicals).
- Inhibition of neurotransmission (organochlorines inhibit the GABA system and cause alteration of calcium homeostasis.
- Uncoupling of oxidative phosphorylation (e.g. glyphosate).
The signs and symptoms of pesticide poisoning depend upon the pesticide involved and the type and magnitude of exposure.

In general the signs and symptoms are:
- dermal and ocular irritation (or allergic response);
- upper and lower respiratory tract irritation;
- allergic responses and asthma;
- gastrointestinal symptoms: usually vomiting, diarrhoea and abdominal pain;
- neurological symptoms: excitatory signs in the case of exposure to organochlorines, lethargy and coma; also polyneuritis;
- specific syndromes:
  - cholinergic crisis (organophosphorus pesticides)
  - bleeding (warfarin-based rodenticides)
  - caustic lesions and pulmonary fibrosis (herbicide, paraquat).

<<NOTE TO USER: Refer to those pesticides commonly used in the country/area.>>
<<NOTE TO USER: insert local photo.>>


Pictures: J. Pronczuk. Lesion caused by paraquat.
"Accidental" ingestion

- Storage of left-over pesticide in a medicine or soft-drink bottle
- Confusion with pharmaceutical
- Pesticide container re-used for storing drinks or food
- Pesticide container present in the child's environment

Acute poisoning results from "accidental" (non-intentional) exposure in toddlers and small children.

Ingestion occurs, for example, when:

- Pesticides have been stored in a medicine or soft-drink bottle.
- The pesticide bottle is similar to a bottle used for pharmaceuticals.
- Pesticide containers are re-used for storing drinks or food.
- Pesticide containers are easily accessible in the child's environment.
**Pesticides and Children**

**ACUTE POISONING**

**Arizona Household Survey**

- 107 homes surveyed:
  - 148 different pesticide products
  - half were stored inside
  - less than 1.2 m from ground
  - in the kitchen

<< NOTE TO USER: Add local data on number of children affected by acute pesticide-related illnesses in your region. Refer to data from the Poison Centre, Ministry of Health, local hospital or other relevant source of local information.>>

For example: around 50% of all reported acute pesticide poisonings reported in the USA involve children under 6 years old.

Pesticides are easily accessible in many houses.

A survey in the state of Arizona identified 148 pesticide products in the 107 houses surveyed. Half of the pesticides were stored inside the home, less than 4 feet (1.22 cm) from the ground, mainly in the kitchen.

Refs:

*Picture: EPA. Milk stored next to flask of insecticide.*
The diagnosis is based upon the history of exposure (e.g. pesticides are available in the home, recently applied, or child was found playing with containers), signs and symptoms of exposure (see next slides) and laboratory measurements. Diagnosis also requires a high index of suspicion. Even after acute exposures, pesticide poisoning may be misdiagnosed as a viral illness (e.g. infectious diarrhoea rather than organophosphate poisoning) resulting in inadequate treatment and potentially returning children to a setting where exposure will be ongoing or recur.

Pesticides and/or their metabolites may be measured in samples of blood, urine, breast milk, amniotic fluid or meconium. This can confirm the diagnosis.

Laboratory tests are available to assess exposure to organophosphates, organochlorine, dicarboximide fungicides, carbamates, dipyridyl herbicides (e.g. paraquat) and pyrethroids.

Ref:

### Pesticides and Children

#### ACUTE TOXINDROMES

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<tr>
<th>PESTICIDE</th>
<th>ACUTE SYMPTOMS</th>
<th>DIAGNOSIS</th>
<th>TREATMENT</th>
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<tr>
<td><strong>Organo phosphates</strong>&lt;br&gt;Clorpyriphos&lt;br&gt;Diazinon&lt;br&gt;Azinphos&lt;br&gt;Parathion</td>
<td>Irreversible cholinesterase inhibition&lt;br&gt;Cholinergic crisis:&lt;br&gt;- nausea, vomiting&lt;br&gt;- hypersecretion&lt;br&gt;- miosis&lt;br&gt;- fasciculations&lt;br&gt;- coma</td>
<td>Cholinesterase levels (red blood cells)</td>
<td>- Supportive care&lt;br&gt;- Atropine i/v&lt;br&gt;- Oximes&lt;br&gt;- Decontamination</td>
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<tr>
<td><strong>Carbamates</strong>&lt;br&gt;Carbaryl&lt;br&gt;Aldicarb</td>
<td>Reversible cholinesterase inhibition</td>
<td>Cholinesterase levels (RBC)</td>
<td>- Supportive care&lt;br&gt;- Atropine i/v&lt;br&gt;- Decontamination</td>
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<<READ SLIDE.>>

## Pesticides and Children

### ACUTE TOXINDROMES

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<td><strong>Pyrethroids</strong></td>
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<td>Type I</td>
<td>Allethrin - Tremor - Ataxia - Irritability</td>
<td>urinary 3-phenoxybenzoic acid is measured in research studies</td>
<td>Supportive care - Symptomatic - Decontamination</td>
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<td>Tetramethrin</td>
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<td>Type II</td>
<td>Deltamethrin - Salivation - Temporary paresthesias - Seizures</td>
<td>urinary 3-phenoxybenzoic acid is measured in research studies</td>
<td>Supportive care - Symptomatic - Decontamination</td>
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<td><strong>Organo chlorines</strong></td>
<td>Lindane - GABA blockade: - Tremors - Dizziness - Seizures</td>
<td>Detectable in blood</td>
<td>Supportive care - Symptomatic - Decontamination</td>
</tr>
<tr>
<td></td>
<td>Endosulfan</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<<READ SLIDE.>>


*Ref:*

## ACUTE PESTICIDE TOXINDROMES

<table>
<thead>
<tr>
<th>PESTICIDE</th>
<th>ACUTE SYMPTOMS</th>
<th>DIAGNOSIS</th>
<th>TREATMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorophenoxi compounds</td>
<td>Nausea, vomiting, acidosis, myalgia, fever, myopathy, neurophytis</td>
<td>Detectable in urine</td>
<td>Decontamination and urine alkalization</td>
</tr>
<tr>
<td>(e.g: 2,4 D)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bipyridyl compounds</td>
<td>Vomiting, corrosive lesions, hepatotoxicity, acute tubular necrosis, pulmonar fibrosis</td>
<td>Dithionite test in urine</td>
<td>Decontamination, avoid O2, hemoperfusion, possibly: corticosteroids and ciclophosphamide</td>
</tr>
<tr>
<td>paraquat</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anticoagulant Rodenticide</td>
<td>Haemorrhage (from vit. K antagonism)</td>
<td>Elevated protrombine time (PT)</td>
<td>Vitamin K1 (fitomenadione)</td>
</tr>
<tr>
<td>Warfarine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brodifacoum</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Diphacinone</td>
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</tr>
</tbody>
</table>

<<READ SLIDE.>>

Pesticides and Children

LOW-LEVEL CHRONIC EXPOSURE

Growing body of epidemiological and animal data and research studies suggest a link between long-term exposure and:

- Abnormal growth and development
- Impaired neurological development
- Cancer
- Increased susceptibility to infections

The mechanisms of action thought to produce chronic toxic effects include genotoxicity, endocrine disruption and immunotoxicity. Effects may be seen when exposure occurs during critical windows of development, particularly the prenatal period. See following slides.

Ref:
Preconceptional prenatal exposure

Pesticide exposure before or during pregnancy associated with increased risk of:
- Infertility
- Perinatal death
- Spontaneous abortion
- Premature birth
- Fetal growth retardation
- Congenital malformations
- Early childhood cancer

Exposure of either mother or father to pesticide before conception, or exposure of the mother during pregnancy, has been associated with an increased risk of fetal death, spontaneous abortion and early childhood cancer.

There is increasing evidence that in utero exposure increases the risk of growth retardation: a small-for-gestational age baby, low birth weight, reduced length and small head circumference (see photo).

Significant increases in the risk of congenital anomalies have also been reported. These include: eye defects, limb reduction, urogenital defects, hypospadias, cryptorchidism, orofacial clefts, central nervous system defects and heart defects.

Refs:
Exposure during brain growth has subtle and permanent effects on:

- Brain structure and function
- Neuronal and axonal differentiation
- Serotoninergic system
- Synaptogenesis
- Programming of synaptic function

Exposure during brain growth may exert subtle, permanent effects on the structure and function of the brain. These include:

- neuronal and axonal differentiation;
- alteration of serotoninergic system; and
- altered synaptogenesis and programming of synaptic function.


The appropriate regulation of drugs, chemicals and environmental contaminants requires the establishment of clear and accepted guidelines for developmental neurotoxicity. Ideally, these guidelines should encompass the ability to assess widely disparate classes of compounds through routine tests, with high throughput and low cost. Increasingly, however, the progress in primary research from academic laboratories deviates from this goal, focusing instead on categorizing novel effects of toxicants, development of new testing paradigms, and extension of techniques into molecular biology. The differing objectives of academic science as opposed to those of regulatory agencies or industry, are driven in part, by the priorities of the agencies that fund primary research. Recent work on organophosphate pesticides (OPs) such as chlorpyrifos (CPF) illustrate this dichotomy. Originally, OPs were thought to affect brain development through their ability to elicit cholinesterase inhibition and consequent cholinergic hyperstimulation. This common mechanism allowed for parallels to be drawn between standard measures of systemic toxicity, gross morphological examinations, and exposure testing utilizing an easily-assessed surrogate end-point, plasma cholinesterase activity. In the past decade, however, it has become increasingly evident that CPF, and probably other OPs, have direct effects on cellular processes that are unique to brain development, and that these effects are mechanistically unrelated to inhibition of cholinesterase. The identification and pursuit of these mechanisms and their consequences for brain development represent new and exciting scientific findings, while at the same obscuring the ability to sustain a uniform approach to neurotoxicity guidelines or biomarkers of exposure. In the future, a new set of test paradigms, relying on primary work in cell culture, invertebrates, or non-mammalian models, followed by more targeted examinations of specific processes in mammalian models, may unite cutting-edge academic research with the need for establishing flexible guidelines for developmental neurotoxicity.
Mechanisms of developmental toxicity may be different from those of acute toxicity. For example: chlorpyrifos and cholinergic systems.

- Parent compound is also toxic
- Non-cholinergic systems are primary targets too

Acetylcholinesterases are enzymes that play a direct role in axonal outgrowth and neuronal differentiation. Exposure to organophosphorus pesticides inhibits the enzymes and may therefore interfere with this function. The pesticides chlorpyrifos and diazinon alter axonogenesis, synaptogenesis and programming of synaptic functions. The mechanisms of action postulated are: serotonergic system alteration and inhibition of ARN synthesis in neurones and glial cells. Data suggest that some of the toxicity is from the parent compound rather than the active metabolite and occurs independently of the cholinergic systems that are responsible for acute toxicity.

And, these neurodevelopmental toxicities occur at exposure levels too low to cause overt symptoms of cholinesterase inhibition in the pregnant animals.

Refs:
It may be difficult to differentiate the effects of prenatal exposure from those of chronic low-level exposure in early childhood, or sequelae of non-fatal acute poisonings.

Chronic neurobehavioural and neurological effects after acute poisoning with organophosphorus pesticides have been reported in adults.

Memory and concentration problems, unusual fatigue, irritability and depression, visual difficulties and delayed polyneuropathy have been described.

In a well-documented case of chronic organophosphorus pesticide poisoning, the house of an infant with hypertonia, first diagnosed as cerebral palsy, was found to have high levels of chlorpyrifos weeks after a professional application (Wagner, 1994).

Few studies have examined the neurobehavioural effects of postnatal exposure to pesticides.

Subtle changes in short-term memory and attention may be associated with application of organophosphorus pesticides in the home.

There is increasing evidence, particularly from animal models, about neurobehavioural effects of long-term exposure to low levels of pesticides, such as from pesticides found in food, in indoor air or in the home.

Mental and emotional symptoms have been described in adolescents exposed to aerial spraying of pesticides.


PESTICIDES AND CHILDHOOD CANCER

Some studies have found an association between postnatal pesticide exposure and paediatric cancer

- Brain tumours
- Acute lymphocytic leukaemia
- Non-Hodgkin lymphoma

A number of epidemiological studies have found a significant association between cancer and domestic exposure to pesticides. Evidence is increasing, but still limited because of the methodological weaknesses of the research. Investigations in children living in the rural areas of developed countries have also produced limited evidence.

Refs:
Prenatal exposure has been associated with leukaemia in a newborn after intensive use of permethrin at home by the pregnant mother. Children with certain metabolic enzyme polymorphisms have an increased risk of acute lymphocytic leukaemia when exposed to pesticides in utero or during pregnancy (particularly 2,4-D herbicide). Brain cancer appears to be associated to maternal exposure during agricultural activities. There are some controversial studies that suggest an increased risk of cancer in children whose parents had occupational exposure to pesticides.

Refs:
Pesticides and Children

ENDOCRINE DISRUPTION

- Low doses of certain pesticides may mimic or block hormones or trigger inappropriate hormone activity
- Endocrine disruption may alter development and reproduction and induce birth defects
  - Infertility
  - Low sperm count
  - Early puberty
  - Hormone-dependent cancers (testicular, breast, prostate)
  - Altered sex ratio

Endocrine disruption is not an effect, but a *mechanism* of toxicity that may have different effects.

Evidence of the effect related to this mode of toxicity in children is still limited.

There is experimental evidence of endocrine disruption. Pesticides may have:

- estrogenic effects (DDT, dieldrin, endosulfan, methoxychlor)
- anti-androgenic effects (DDT, vinclozolin, procymidone)
- anti-thyroid effects (ethylenethiourea (ETU), maneb, zineb metabolites)
- anti-progestin effects (DDT).

Synthetic pesticides may interfere with the natural process of development.

Refs:

Pesticides and Children

IMMUNOTOXICITY

- Immunotoxicity is suspected, but evidence is limited

Studies in Arctic zone:

- Higher incidence of ear infections
- Cytokine panel abnormalities

Evidence on the immunotoxic mode of action and effects is limited. Studies from the Arctic zone and Europe are beginning to provide some evidence. Children contaminated with chlordane and heptachlor had cytokine panel abnormalities.

Inuit infants from the Artic zone exposed in utero and to breast milk contaminated with \( p,p' \)-DDE, hexachlorobenzene and dieldrin had a higher incidence of otitis media.

Refs:


Picture:

www.smithsonianmag.si.edu/smithsonian/issues04/jan04/images/topdogs_mush_jpg.html - Copyright © Smithsonian Institution, 2002. All rights reserved.
This summary slide shows the complexity of the issues related to children's environmental exposure to pesticides and the effects on their health.

Pesticides used in agriculture, treatment of animals, on lawns, and for protection of human and public health may enter the air, food, water and soil in the places where children spend most of their time (e.g. at home, at school, in playgrounds, on farms and in fields) and may also contaminate their toys, floors, carpets and materials in their playgrounds.

Children become exposed by:
• eating and drinking contaminated food and beverages;
• playing in contaminated areas;
• gaining access to unsafely stored pesticides, or pesticides stored in attractive, colourful containers; and
• helping in the house and on the farm or as child labour.

Children have special susceptibilities related to:
• critical windows of susceptibility;
• age;
• nutritional status; and
• poverty.

Exposure may lead to:
• acute effects including irritation of the skin or eyes, coughing, lacrimation;
• poisoning, with systemic effects;
• neurotoxicity;
• impaired development;
• endocrine disruption; and
• cancer.

<<NOTE TO USER: You may wish to replace this photo with an appropriate image of a child/children from your region.>>

Picture on the left: WHO, C. Gaggero. Jamaica, Nutrition and child
Because of the potential for long-term damage to critical structures such as the nervous system, immune system and endocrine system, prevention of all acute poisoning events as well as of exposure to low doses during development is a high priority for ensuring children’s environmental health. There are many steps that can be taken at the local/practice level, national/government level and international treaty/trade levels to decrease exposure to pesticides and related illnesses.

*Picture: WHO, L. De Toledo. Ethiopia*
Pesticides and Children

PREVENTION – LOCAL LEVEL

Use pesticides ONLY when the benefits outweigh the risks
- Avoid cosmetic or scheduled use of pesticides in the home
- Use integrated pest management (IPM), non-chemical pest controls

If pesticides are necessary:
- Store in original containers with child-proof seals, out of reach, in a locked cabinet
- Educate on the safe use of pesticides
  - Follow manufacturer’s instructions
  - Use protective equipment
  - Respect re-entry times
  - Pregnant women should not apply pesticides
- Use least hazardous chemicals, least dangerous mode of application

Pesticides should be used only when the benefits outweigh the risks, and non-chemical pest control procedures have failed.

Cosmetic use of pesticides, that is their use to control aesthetically unpleasant plants or non-dangerous insects such as crickets or house millipedes, should be completely avoided.

Integrated pest management (IPM) procedures which include hygiene, sealing of cracks and crevices, screening of doors and windows, and other measures should be the first line of defence for pest management.

If pesticides must be used, they should be stored only in their original containers with manufacturer's labels intact, preferably with child-proof seals, out of the reach of children and in locked cabinets or cupboards.

Users should always follow the safety precautions specified by the manufacturer and observe all safety recommendations including use of gloves, masks, protective clothing and observation of re-entry times (the time when it is safe to return to a treated area).

Pregnant women should not apply pesticides and particular care should be taken to determine appropriate re-entry times for pregnant women, infants and small children. These times may be considerably longer than for less vulnerable individuals.

If chemicals are required, the least hazardous chemical (when there is scientific evidence of less toxicity) should be used with the most contained mode of distribution considered effective. For example, fogs and bombs should not be used. Bait stations are preferable to baseboard sprays or crack and crevice treatment. Granules and bait stations should be used only if they are inaccessible to babies, toddlers and small children (and pets).


Pesticides and Children

PREVENTION – COMMUNITY LEVEL

- Integrated pest management (IPM)
  - Homes
  - Schools
  - Public buildings
  - Health centres
  - Public parks

- Community activities
  - Community campaigns
  - School activities
  - Local awards or contests
  - Pesticide-free "zones"
  - Support organic farming

Many organizations (especially FAO and WHO) promote alternative non-chemical forms of pest-control and there is increasing engagement in non-pesticide dependent agriculture and integrated pest management (IPM).

A variety of local initiatives involving the community can help to create an environment that promotes decreased dependence on pesticides in homes, schools, public areas, health facilities and parks.

Examples of community activities include:
- community campaigns and school activities;
- local awards or contests;
- pesticide-free "zones"; and
- support for organic farming.

<<READ SLIDE.>>

Pesticides and Children

PREVENTION – NATIONAL LEVEL

- Education campaigns aimed at pesticide users, general population and children
- Restrict availability or limit use
- Establish and monitor maximum residue limits
- Surveillance and epidemiological vigilance for acute and chronic related illness
- Treatment capacities
  - Emergency services
  - Poison control centres
  - Education of health care providers

Education is a key component of safe pesticide use and prevention of toxic exposures. Farmers, pesticide applicators and their families need to be informed and educated on how to recognize and prevent pesticide poisonings. Trained or licensed pesticide applicators can maximize preventive measures.

Bans and restrictions on use of pesticides found to be highly toxic or persistent in the environment have been successful; severe poisonings are seen less frequently than in the past. For example, organochlorine poisoning no longer occurs in countries that restrict their uses to a specific agricultural application and have banned domestic use.

A major change in regulatory approaches to pesticides occurred when the US Congress passed the Food Quality Protection Act in 1996. This law requires the US EPA to set residue levels for foods to protect the most vulnerable populations, specifically infants, children and fetuses (pregnant mothers) from harm due to cumulative exposure taking into account all routes of exposure. This law has led to the restrictions on use and voluntary withdrawal from the market by manufacturers of several previously widely used pesticides (e.g. chlorpyrifos and diazinon).

Pesticide manufacturers and governments should follow the voluntary FAO International Code of Conduct on the Distribution and Use of Pesticides.

•USEPA Website Food Quality Protection Act, 1996 (www.epa.gov/oppfead1/fqpa/backgrnd.htm).
Nine of the 12 persistent organic pollutants (POPs) included in the Stockholm Convention, are pesticides (aldrin, chlordane, DDT, dieldrin, endrin, heptachlor, mirex, toxaphene and hexachlorobenzene). This convention, under the auspices of United Nations Environmental Programme became effective in May 2004, after it was signed by 50 countries.

The Rotterdam Convention on the Prior Informed Consent (PIC) procedure for certain hazardous chemicals and pesticides was adopted in September 1998, and has been signed by 73 countries. The convention establishes a first line of defence against toxic chemicals, giving importing countries the power to receive information and decide which potentially hazardous chemicals they want to receive. It also covers labelling requirements. The convention includes 22 pesticides.

Other international organizations such as the Intergovernmental Forum for Chemical Safety (IFCS), the International Labour Organization (ILO) and others are working towards safer use and monitoring of pesticides at the global level.

Refs:
• www.pic.int
PESTICIDES AND CHILDREN: ACTIVITIES IN WHO

1. Guidelines for the classification of pesticides by hazard
2. Joint FAO/WHO Meeting on Pesticide Residues
3. International pesticide limits in water
4. Pesticides Databank on CD-ROM
5. Poison centres and pesticide exposures

1. WHO guidelines for the classification of pesticides by hazard. The WHO Recommended Classification of Pesticides by Hazard was approved by the 28th World Health assembly in 1975 and has since gained worldwide acceptance. Guidelines were first issued in 1978, and have since been revised and reissued at 2-yearly intervals. Ref: IPCS. The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 2000-2002. Geneva, World Health Organization, 2002.

2. The Joint FAO/WHO Meeting on Pesticide Residues (JMPR) is an international expert scientific group that is administered jointly by the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO). JMPR, which consists of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group, has been meeting regularly since 1963. During the meetings, the FAO Panel of Experts is responsible for reviewing information on residues and analytical aspects of the pesticides under consideration, including data on their metabolism, fate in the environment, and use patterns, and for estimating the maximum levels of residues that might occur as a result of the use of the pesticides according to good agricultural practices. The WHO Core Assessment Group is responsible for reviewing toxicological and related data and for estimating, where possible, acceptable daily intakes (ADIs) for humans of the pesticides under consideration. Ref: www.who.int/ipcs/food/jmpr/en

The Codex Alimentarius Commission was created in 1963 by FAO and WHO to develop food standards, guidelines and related texts such as codes of practice under the Joint FAO/WHO Food Standards Programme. The main purposes of this Programme are protecting the health of the consumers and ensuring fair trade practices in the food trade, and promoting coordination of all work on food standards undertaken by international governmental and nongovernmental organizations. Ref: www.codexalimentarius.net/web/index_en.jsp


4. The Pesticides Databank on CD-ROM holds a collection of internationally peer-reviewed documents on risk assessments of pesticides and poisons, information monographs, the updated IPCS Manual on Diagnosis and Treatment of Pesticide Poisonings, a distance-learning module on prevention, diagnosis and management of pesticide poisoning, aimed at three levels of user: community physicians, agricultural workers and the general public. Available at IPCS (WHO).

5. Poison centres play a key role in providing information, advice and management of case of pesticide exposure in the countries where they are available. For more information, see: www.who.int/ipcs/poisons/centre/directory/en/
Health and environment professionals have a critical role to play in maintaining and stimulating changes that will restore and protect children’s environmental health, and protect them from pesticide exposure.

Health care providers can do something. At the one-to-one level with the patient, they can include pesticide poisoning in the differential diagnoses and in preventive advice. They can be dissatisfied with the diagnosis of “idiopathic” in cases of paediatric disease and look harder for evidence pointing to pesticides as a potential cause of disease and disability. They can ask specific questions about the use of pesticides within the home, in the garden or farming areas, or about potential pesticide residues in fruit and vegetables. Which pesticides are being used? When? Where? How? What safety and hygiene measures are being taken? Are the instructions being read and followed?

They can publish sentinel cases and develop and write about community-based interventions in relation to pesticides. They can educate patients, families, colleagues and students didactically to diagnose, treat and prevent pesticide poisonings and exposures. They can discourage chemical pesticide use and encourage integrated pest management. They can also provide information about the local Poisons Centre or other sources of information on pesticides.

As professionals with an understanding of both health and the environment, health care providers are powerful role models who can practice integrated pest management, be advocates for strict pesticide laws and regulations, proper labelling of pesticide products and child-proof containers for all pesticide products.
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