

TRAINING FOR THE HEALTH SECTOR

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PESTICIDES

Children's Health and the Environment

WHO Training Package for the Health Sector

World Health Organization

www.who.int/ceh

July 2008 version

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

<<NOTE TO USER: This is a large set of slides from which the presenter should select the most relevant ones to use in a specific presentation. These slides cover many facets of the problem. Present only those slides that apply most directly to the local situation in the region.>>

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

- ❖ **What are pesticides?**
- ❖ **Origin, environmental transport and fate of pesticides**
- ❖ **Routes and circumstances of exposure**
- ❖ **Exposure levels**
- ❖ **Toxicokinetics and toxicodynamics**
- ❖ **Target organs and systems**
- ❖ **Diagnosis and treatment of poisoning**
- ❖ **Prevention of pesticide exposure and poisoning**

<<READ SLIDE.>>

PESTICIDES – RISKS AND BENEFITS

BENEFITS

- ❖ **Crop protection**
- ❖ **Food preservation**
- ❖ **Material preservation**
- ❖ **Disease control**

RISKS

- ❖ **Toxic to humans**
- ❖ **Impact on environment and ecosystems**

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:

•National Resource Council. *Pesticides in the diets of infants and children*. National Academy Press, Washington, DC, 1993.

Pesticides

USE OF PESTICIDES

- ❖ **First use of synthetic pesticides: 1940**
- ❖ **Consumption increasing worldwide**
 - **2.26 million tons of active ingredients used in 2001**
 - **25% of the world production used in developing countries... where 99% of deaths due to pesticides occur!**

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<<READ SLIDE.>>

- a) First use of synthetic pesticides: 1940
- b) Consumption increased substantially over time, for example, 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.
- c) Use has risen in developing countries and the fastest growing markets in Africa, Asia, South and Central America, Eastern Mediterranean. There is a high pesticide use on crops grown for export (Dr. N. Besbelli, WHO, personal communication).
- d) 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.

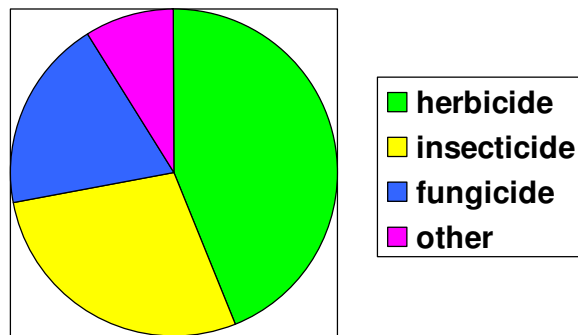
Refs:

- American Academy of Pediatrics Committee on Environmental Health. Pesticides. In: Etzel RA ed. *Pediatric Environmental health*. 2nd ed. Elk Grove Village, American Academy of Pediatrics, 2003.
- Jeyaratnam J. Acute pesticide poisoning: a major global health problem. *World Health Stat Quarterly*, 1990.
- UNEP United Nations Children's Fund and WHO. *Children in the new millennium: environmental impact on health*. UNEP, UNICEF, WHO, 2002.
- US EPA Pesticides industry sales and usage: 2000 & 2001 market estimates: (www.epa.gov/oppbead1/pestsales/01pestsales/market_estimates2001.pdf).
- Vaagt G. *New code of conduct on pesticide adopted*. FAO Newsroom (www.fao.org/english/newsroom/news/2002/10525-en.html).

Pesticides

USE OF PESTICIDES

Global Pesticide Use 2001 (%)



www.epa.gov/oppbead1/pestsales/01pestsales/market_estimates2001.pdf

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The pie chart shows the global use of pesticides and the different types.

Insecticides are mostly used in developing countries and fungicides/herbicides in developed countries.

<<READ SLIDE.>>

Refs:

- American Academy of Pediatrics Committee on Environmental Health. Pesticides. In: Etzel RA ed. *Pediatric Environmental health. 2nd ed.* Elk Grove Village, American Academy of Pediatrics, 2003.
- Jeyaratnam. Acute pesticide poisoning: a major global health problem. *World Health Stat Quarterly*, 1990.
- UNEP United Nations Children's Fund and WHO. *Children in the new millennium: environmental impact on health.* UNEP, UNICEF, WHO, 2002.
- US EPA Pesticides industry sales and usage: 2000 & 2001 market estimates: (www.epa.gov/oppbead1/pestsales/01pestsales/market_estimates2001.pdf).
- Vaagt. *New code of conduct on pesticide adopted.* FAO Newsroom (www.fao.org/english/newsroom/news/2002/10525-en.html).

Pesticides

USE OF PESTICIDES – TYPES OF PRODUCT

- ❖ **Pesticides used in different settings:**
 - Agricultural
 - Veterinary
 - Domestic
 - Institutional
- ❖ **Formulations:** liquid, gel, paste, chalk, powder, granules, pellets, baits...
- ❖ **Concentrations:** from 2% to 80% of active ingredient
- ❖ **Containers:** glass, plastic or metal flasks, bottles, drums, traps, plastic bags or paper bags....

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Pesticides are used in different settings.

<<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. "Chalk" pesticide has been sold illegally in the USA, it may contain pyrethroids. (See US EPA website.)

•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 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:

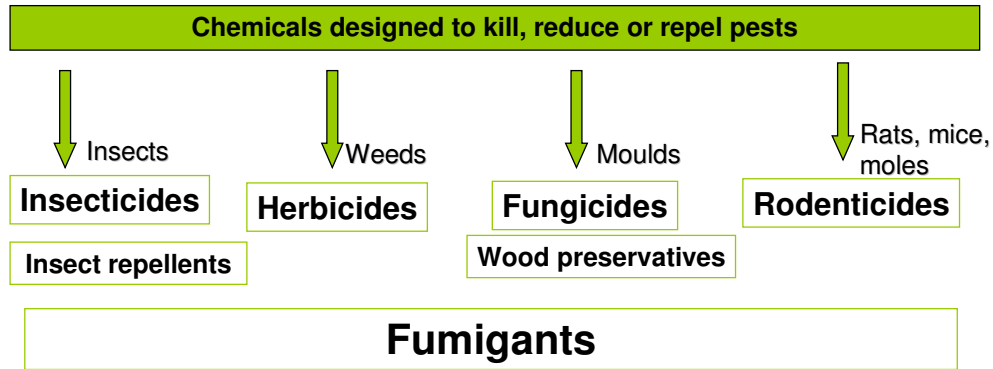
•IPCS. *The WHO Recommended Classification of pesticides by hazard, Guidelines to Classification 2000–2002* (www.inchem.org/documents/pds/pdsother/class.pdf)

•Tomlin C. *The pesticide manual, 11th ed.* British Crop Protection Council Publications, 1997.

•"Chalk" pesticides information at www.epa.gov/opp00001/health/illegalproducts/chalk.htm

Pesticides

PESTICIDES – CLASSIFICATION BY USE



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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).

Pesticides

PESTICIDES – CLASSIFICATION BY USE AND CHEMICAL STRUCTURE

Different chemicals used for different purposes

❖ INSECTICIDES

- Pyrethroids
- Organophosphorus
- Carbamates
- Organochlorine
- Manganese compounds

❖ HERBICIDES

- Bipyridyls
- Chlorophenoxy
- Glyphosate
- Acetanilides
- Triazines

❖ FUNGICIDES

- Thiocarbamates
- Dithiocarbamates
- Cupric salts
- Tiabendazoles
- Triazoles
- Dicarboximides
- Dinitrophenoles
- Organotin compounds
- Miscellaneous

❖ RODENTICIDES

- Warfarines
- Indanodiones

❖ FUMIGANTS

- Aluminium and zinc phosphide
- Methyl bromide
- Ethylene dibromide

❖ INSECT REPELLENTS

- Diethyltoluamide

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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.>>

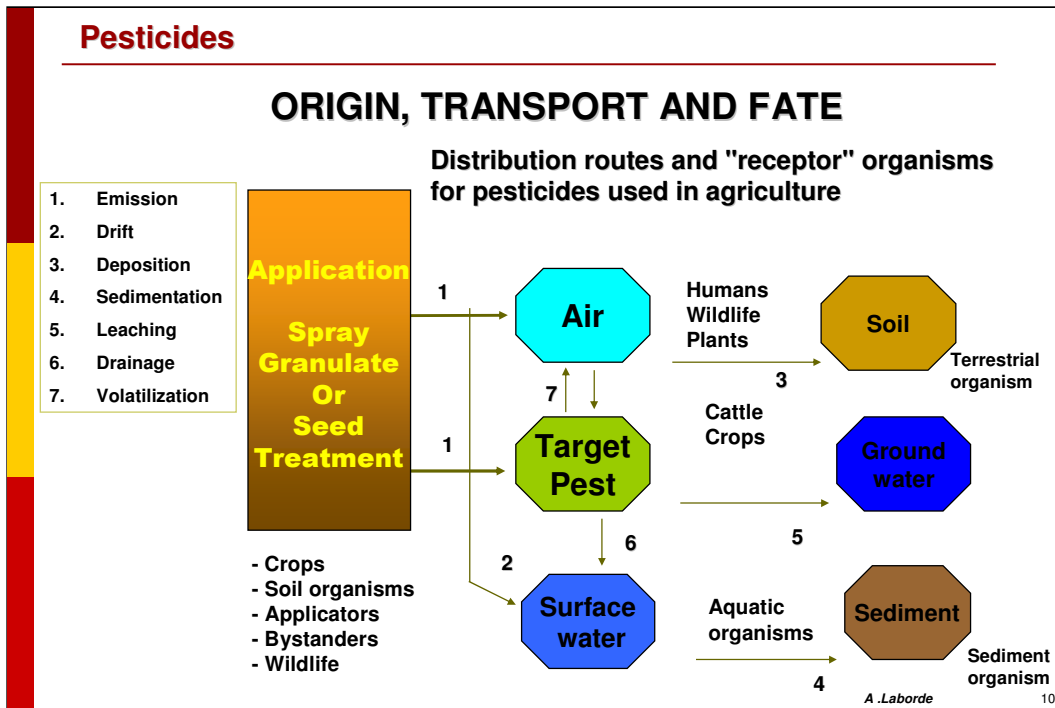
Some domestic, agricultural or veterinary products may contain more than one chemical belonging to the same or a different chemical group.

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 in children 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).

Refs:

- IPCS. *The WHO recommended classification of pesticides by hazard. Guidelines to Classification 2000-2002* (www.inchem.org/documents/pds/pdsother/class.pdf).
- Tomlin C. *The pesticide Manual, 12th ed.* British Crop Protection Council Publications, 2000.



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.

Refs:

•*Children: a CICH profile, 3rd ed.* Canadian Institute of Child Health, 2000.

•Health Canada. *Health and the environment: handbook for health professionals.* Ottawa, Ministry of Public Work and Government Services, 1998.

Pesticides

SOME PESTICIDES PERSIST AND BIOCONCENTRATE

❖ PERSISTENT ORGANIC POLLUTANTS (POPs)

- Low water solubility
- Persist in the environment
- Accumulate in the food-chain
- Lypophilic
- Travel long distances
- Concentrate in marine animals
- May produce toxic effects

PESTICIDES

Aldrin
Dieldrin
Chlordane
DDT
Endrin
Heptachlor
Mirex
Toxaphene

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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 (and PTSs) include industrial chemicals (PCBs, HCB) and unintended byproducts (dibenzodioxins, dibenzofurans), and other chemicals.

•These persistent chemicals are controlled under the Stockholm Convention.

•POPs and PTSs are typically lypophilic compounds, with low water solubility, 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.

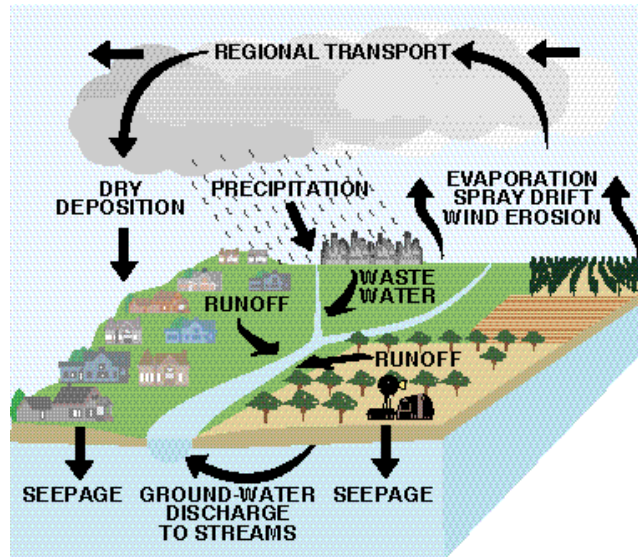
•There is concern about potential endocrine and developmental effects of the POPs and PTSs, especially in children.

Ref:

•Kutz FW et al. Organochlorine pesticides and polychlorinated biphenyls in human adipose tissue. *Rev Environ Contam Toxicol*, 1991, 120:1.

Pesticides

PESTICIDES IN THE ATMOSPHERE AND WATER



USGS

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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

A great potential for adverse effects of pesticides is through contamination of the hydrological system, which supports human life, aquatic life and related food-chains.

Ref:

•USGS: ca.water.usgs.gov/pnsp/atmos/atmos_1.html

Pesticides

EXAMPLE OF SEASONAL PESTICIDE USE

APPLE ORCHARD CALENDAR



NPS

AUTUMN

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

WINTER

- ❖ Fungicides: dinitroorthocresol (DNOC)
- ❖ Insecticides: organophosphate compounds (OPs)

SPRING

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

SUMMER

- ❖ Insecticides: OPs

Ref: Dr A. Laborde, Uruguay

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<<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:

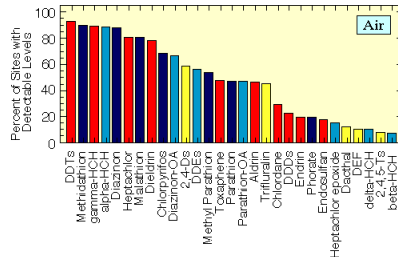
•Achard. Fruit growing calendar. *Banco de Seguros del Estado Yearbook*. Uruguay, 1996.

Picture: www.nps.gov/whmi/gallery/grounds016.htm – NPS – Us Department of the Interior. Apple orchard

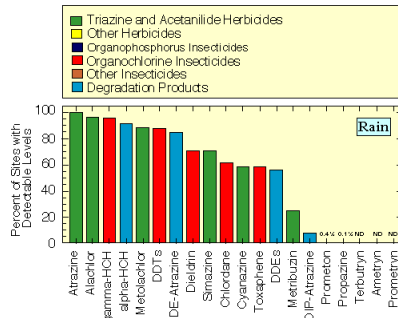
Pesticides

PESTICIDES IN THE ATMOSPHERE

AIR



RAIN



USGS

14

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

CHILDREN'S EXPOSURE

A cause of concern

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



WHO

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Pesticides are considered an important environmental threat to children's health in rural areas. This is 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 may also be heavily used indoors in urban areas, so this is not solely a rural issue.

Pesticides

CHILDREN'S ENVIRONMENTAL EXPOSURE

- ❖ Pesticides in: homes and schools, playgrounds, parks fields, hospitals and other public places
- ❖ Children in: farms, agricultural areas (rural setting)
- ❖ Pesticides present in: air, soil, food, water, parents' clothing and shoes, other objects...

Different scenarios:

- ❖ **ACUTE** high-level exposure, overt poisoning
- ❖ **CHRONIC** low-level, chronic exposure, various effects

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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 used in schools and playgrounds (in treated wood) and in green areas (parks and playing fields) to destroy weeds. Hospitals are intended to be places of healing, yet many are using hazardous pesticides
- Living on farms or in agricultural areas, where pesticides are frequently and heavily used, is a high-risk scenario for exposure.
- Potential for "take home" of pesticides on parents' clothing or shoes.
- 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. (See next slide)

Pesticides

SOURCES AND SETTINGS OF EXPOSURE...

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

Indoor and outdoor application

- ❖ Mosquito control
- ❖ Professional/domestic application

Health uses

- ❖ Lice or scabies
- ❖ Fleas or ticks on pets



WHO

Pesticide residues

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

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A survey by the U.S. Environmental Protection Agency regarding pesticides used in and around the home revealed some significant findings:

- Almost half (47%) of all households with children under the age of five had at least one pesticide stored in an unlocked cabinet, less than 4 feet off the ground (i.e., within the reach of children).
- Approximately 75% of households without children under the age of five also stored pesticides in an unlocked cabinet, less than 4 feet off the ground (i.e., within the reach of children). This number is especially significant because 13% of all pesticide poisoning incidents occur in homes other than the child's home.

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.

Refs:

- www.epa.gov/pesticides/factsheets/childsaf.htm
- Bass JK et al. What is been used at home: a household pesticide survey. *Rev Panam Salud Publica*, 2001, 9:138.
- CDC *Surveillance for acute insecticide related illness associated with mosquito control efforts Nine States 1999–2002* (www.cdc.gov/mmwr/preview/mmwrhtml/mm5227a1.htm).
- Fields S. Caution – children at play: How dangerous is CCA? *EHP*, 2001, 109 A262 (ehp.niehs.nih.gov/docs/2001/109-6/focus.html)
- Forrester MB et al. Epidemiology of lindane exposures for pediculosis reported to poison centers in Texas, 1998–2002. *J Toxicol - Clin Toxicol*, 2004, 42:55.
- Lemus R et al. Chlorpyrifos: an unwelcome pesticide in our homes. *Rev Environ Health*, 2000, 15:421.
- WHO. *The physical school environment, information series on school health, Document 2*. Geneva, World Health Organization, 2003.

Picture: WHO

Pesticides

Historical use of DDT...



Norsk Barnemuseum

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Fig: Norsk Barnemuseum. www.norskbarne.museum.no/html/barn100.htm Used with copyright permission.

Pesticides

SOURCES AND SETTINGS OF EXPOSURE

Children living on farms or in agricultural areas are exposed to:

- ❖ pesticide drift from sprayed fields
- ❖ contaminated dust & soil
- ❖ contaminated equipment and clothes
- ❖ treated fields
- ❖ parents spraying
- ❖ animal dips
- ❖ child labour



Corra

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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 to the fields 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.

Refs:

•Calvert GM et al. Acute pesticide-related illnesses among working youths, 1988-1999. *Am J. Public Health* 2003, 93: 605.

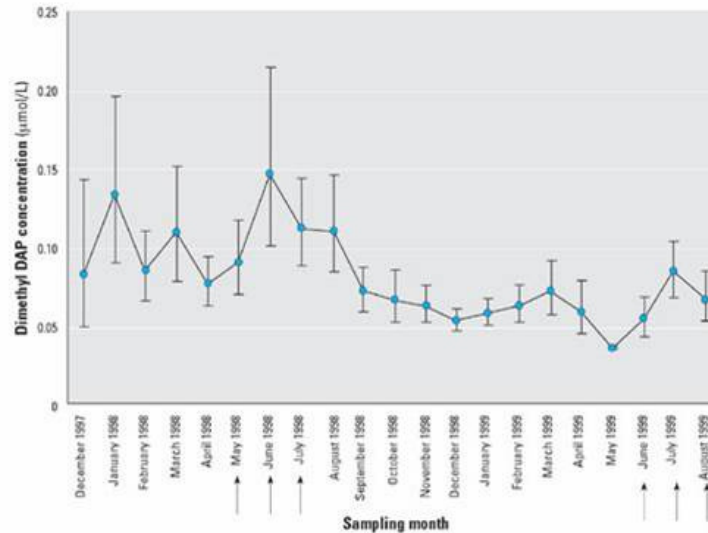
•Quandt SA et al. Agricultural and residential pesticides in wipe samples from farmworker family residences in North Carolina and Virginia. *Environ Health Perspect*, 2004, 112:382.

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

Pesticides

CHILDREN'S EXPOSURE IN RURAL SETTINGS

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



Koch *EHP*, 2002, 110 (8): 829

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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.

Refs:

•Aprea C et al. Biologic monitoring of exposure to organophosphorus pesticides in 195 Italian children. *Env Health Perspect*, 2000, 108:521.

•Koch D et al. Temporal association of children's pesticide exposure and agricultural spraying: report of a longitudinal biological monitoring study. *Env Health Perspect*, 2002, 110:829.

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 dialkylphosphate (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.

•Loewenherz C et al. Biological monitoring of organophosphorus pesticide exposure among children of agricultural workers in Central Washington State. *Environ Health Persp* 1997, 105:1344.

Figure: ehp.niehs.nih.gov/members/2002/110p829-833koch/koch-full.html

Reproduced with permission from *Environmental Health Perspectives*

PESTICIDES IN DIFFERENT MEDIA

Air

- ❖ **Respirable particles contaminated with pesticides**
- ❖ **Respirable aerosols during spraying**
- ❖ **Vapour from volatile residues of pesticides**

Soil

- ❖ **Hand-to-mouth behaviour**
- ❖ **Crawling on the ground**
- ❖ **Dermal contact**

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 micrometres 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 activities) facilitates exposure.

Pesticides

PESTICIDES IN DIFFERENT MEDIA

Water

- ❖ Pesticides in drinking water: tap, well

Food

- ❖ Crops routinely sprayed:
 - fruits, vegetables, grains
- ❖ Bioaccumulation in animals and products
 - fish, meat, eggs, dairy



WHO

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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. Please note that the benefits to children of a diet rich in fruits and vegetables should be emphasized. There are preventive and regulatory measures on this issue. (See additional slides)

Picture: WHO, C. Gaggero. Nutrition child, Peru.

<<READ SLIDE.>>

Pesticides

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: acceptable daily intake (ADI)



WHO 23

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) and to understand the effect of multiple exposures.

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:

- American Academy of Pediatrics Committee on Environmental Health. Pesticides. Chapter 24. In: Etzel RA. ed. *Pediatric Environmental Health 2nd Ed.* Elk Grove Village IL, American Academy of Pediatrics, 2003.
- Fenske R et al. Biologically based pesticide dose estimates for children in an agricultural community. *Environ Health Perspect* 2000, 108:515.
- Jensen AF et al. Cumulative Risk assessment of the intake of organophosphorus and carbamate pesticides in the Danish diet. *Food Addit. Contam*, 2003, 20:776.
- Rhorer. Transfer efficiencies of pesticides from household flooring surfaces to food. *J Exp Anal Environ Epidem* 2003, 13:454.
- Sanborn MD et al. Identifying and managing adverse environmental health effects: 4 Pesticides. *CMAJ*, 2002, 166:1431.
- 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

Pesticides

TOXICOKINETICS VARIES FOR DIFFERENT TYPES OF PESTICIDE

Important to consider:

❖ Routes of Absorption

- Dermal, ocular, ingestion, inhalation, injection

❖ Biotransformation

- Into inactive or more active metabolites

❖ Distribution and storage

- Fat soluble pesticides are stored in adipose tissue
- Other

❖ Elimination

- Urinary excretion
- Biliary / faecal excretion
- Excretion in milk

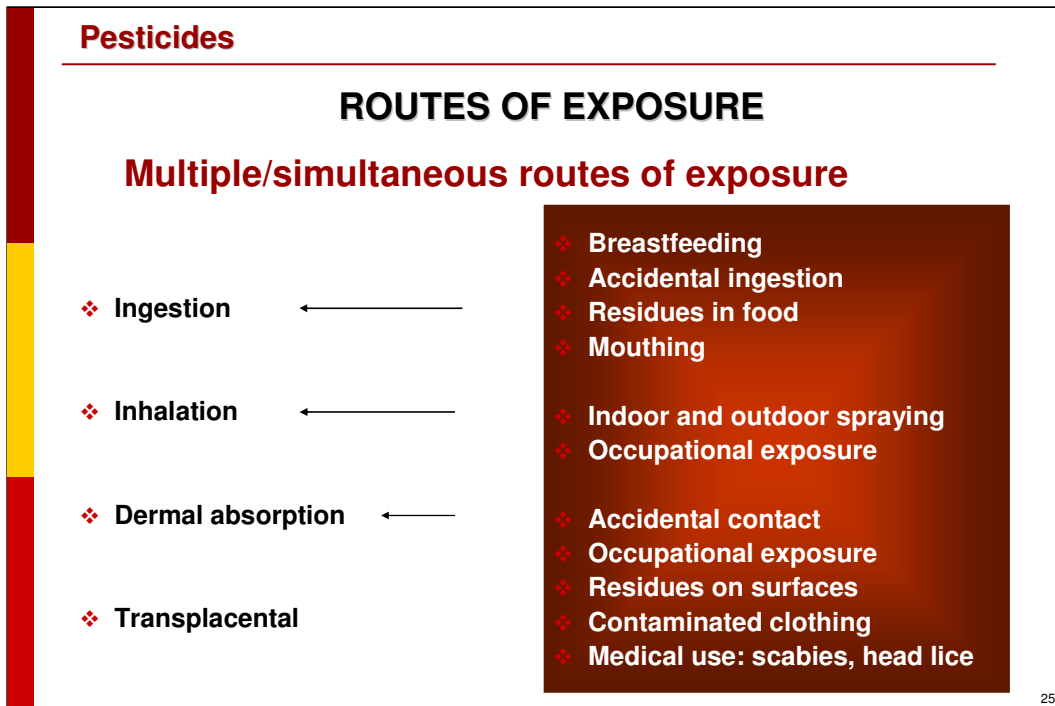
24

Toxicokinetics depend on the specific pesticide, its chemical characteristics and formulation. 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:

• Hodgson. Metabolism. In: *Hayes, Handbook of pesticide toxicology*. San Diego California, Academic Press Inc. 1991.



Almost all pesticides are absorbed by these routes.

<<READ SLIDE.>>

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. Modifying diets and assuming their variety could be a way of reducing exposures...

Ref:

•Health Council of the Netherlands. *Pesticides in food: assessing the risk to children*. The Hague: Health Council of the Netherlands, 2004.

ROUTES OF PERINATAL EXPOSURE

- ❖ **Mother's intake and body burden is transferred across the placenta**
- ❖ **Breast milk may be contaminated**
"The very top of the food chain"



WHO

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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 compounds (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.
- There is currently no developed method to measure OPs in breast milk.
(Please see the module on Children and Chemicals.)

Refs:

- Pronczuk J et al. Global perspectives in breast milk contamination infectious and toxic hazards. *Environ Health Perspect*, 2002, 110:A349.
- Whyatt RM et al. Measurement of organophosphate metabolites in postpartum meconium as a potential biomarker of prenatal exposure. A validation study. *Env Health Perspect*, 2001, 109:417.

Picture: WHO, P. Viro. Portrait of a young baby breastfeeding, Delhi, India, Asia, November 2002.

Pesticides

METABOLIC PATHWAYS

❖ Organophosphates metabolize into:

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

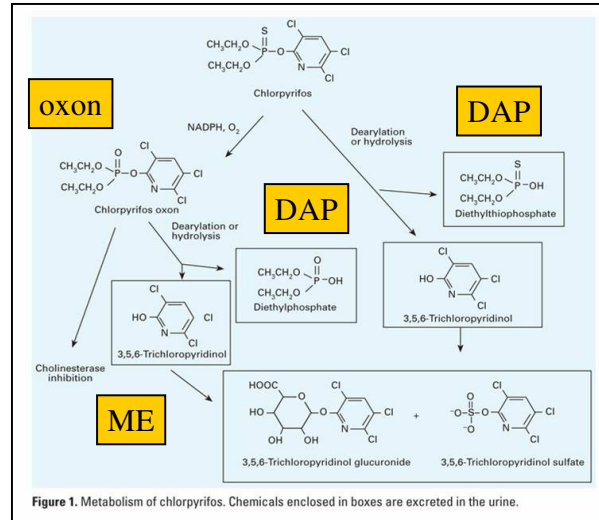


Figure 1. Metabolism of chlorpyrifos. Chemicals enclosed in boxes are excreted in the urine.

Wessels, EHP (2003) 111 (16): 1939

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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:

•Wessels D et al. Use of biomarkers to indicate exposure of children to organophosphate pesticides: implications for a longitudinal study of children's environmental health. *Environmental Health Perspectives*, 2003, 111:1939.

Figure: Reproduced with permission from *Environmental Health Perspectives*

MECHANISMS OF ACUTE TOXICITY

- ❖ Irritation (most of the pesticides)
- ❖ Allergic sensitization (e.g. fungicides)
- ❖ Enzyme inhibition (e.g. cholinesterases and OPs & carbamates)
- ❖ Oxidative damage (e.g. paraquat)
- ❖ Inhibition of neurotransmission (e.g. organochlorines)
 - Calcium (Ca^{2+}) homeostasis alteration
 - GABA inhibition
- ❖ Uncoupling of oxidative phosphorylation (e.g. glyphosate)

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 organophosphorus compounds and carbamates).
- 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).

OP: organophosphorus compounds

Pesticides

ACUTE PESTICIDE-RELATED ILLNESS

- ❖ Dermal and ocular irritation (or allergic response)
- ❖ Upper and lower respiratory tract irritation
- ❖ Allergic responses / asthma (fungicides)
- ❖ Gastrointestinal symptoms
- ❖ Neurological symptoms
- ❖ Specific syndromes
 - Cholinergic crisis (organophosphorus pesticides)
 - Bleeding (warfarin-based rodenticides)
 - Caustic lesions and pulmonary fibrosis (herbicide, paraquat)



Paraquat lesions courtesy of Dr. J. Pronczuk

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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 (paraquat)

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

<<NOTE TO USER: insert local photo.>>

<<READ SLIDE.>>

Refs:

- American Academy of Pediatrics Committee on Environmental Health. Pesticides. Chapter 24. In: Etzel RA. ed. *Pediatric Environmental Health, 2nd Ed.* Elk Grove Village IL. American Academy of Pediatrics, 2003.
 - CDC. Surveillance for acute insecticide-related illness associated with mosquito-control efforts--nine states, 1999–2002. *MMWR Morb Mortal Wkly Rep*, 2003, 52:629.
 - Salameh PR et al. Respiratory symptoms in children and exposure to pesticides. *Eur Respir J*, 2003, 22:507.
 - Sanborn MD et al. Identifying and managing adverse effects: 4 Pesticides. *CMAJ*, 2002, 166:1431.
- Pictures: Courtesy of Dr. J. Pronczuk. Lesion caused by paraquat.*

Pesticides

ACUTE POISONING BY "ACCIDENTAL" INGESTION

- ❖ Storage of leftover pesticide in a medicine or soft drink bottle
- ❖ Confusion with pharmaceutical
- ❖ Pesticide container reused for storing drinks or food
- ❖ Pesticide container present in the child's environment



Bottles containing pharmaceuticals and the pesticide chlorpyrifos
Laborde, CIAT, Montevideo

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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 reused for storing drinks or food.
- Pesticide containers are easily accessible in the child's environment.

Photo: Bottles containing pharmaceuticals and the pesticide chlorpyrifos
Courtesy of Laborde, CIAT, Montevideo

DIAGNOSIS OF EXPOSURE

- ❖ **History of exposure**
 - Availability of pesticides
 - Recent application
- ❖ **Signs and symptoms**
 - May be misdiagnosed!
- ❖ **Laboratory tests**



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<<READ SLIDE.>>

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 can 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:

•American Academy of Pediatrics Committee on Environmental Health. Pesticides. Chapter 24. In: Etzel RA. ed. *Pediatric Environmental Health*, 2nd Ed. Elk Grove Village IL. American Academy of Paediatrics, 2003.

Picture: WHO, C. Gaggero. Health child examination, Peru.

Pesticides

ACUTE TOXINDROMES

PESTICIDE	ACUTE SYMPTOMS	DIAGNOSIS	TREATMENT
Organo phosphorous E.g. Clorpyrifos Diazinon Azinphos Parathion	"Irreversible" cholinesterase inhibition Cholinergic crisis: - nausea, vomiting - hypersecretion - miosis - fasciculations - coma	Low cholinesterase levels in red blood cells (RBC)	- Supportive care - Atropine i/v - Oximes - Decontamination
Carbamates E.g. Carbaryl Aldicarb	Reversible cholinesterase inhibition	Low cholinesterase levels (in RBC)	- Supportive care - Atropine i/v - Decontamination

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<<READ SLIDE.>>

Modified from Table of American Academy of Pediatrics, Committee on Environmental Health. In: Etzel, R. ed. *Paediatric Environmental Health 2nd Ed.* Elk Grove Village IL, 2003.

Pesticides

ACUTE TOXINDROMES

PESTICIDE	ACUTE SYMPTOMS	DIAGNOSIS	TREATMENT
Pyrethroids			
Type I E.g. Allethrin Permethrin Tetramethrin	- Tremor - Ataxia - Irritability	- Urinary 3-phenoxybenzoic acid (in research studies)	- Supportive care - Symptomatic - Decontamination
Type II E.g. Deltamethrin Cypermethrin Fenvalerate	- Salivation - Temporary paraesthesias - Seizures	- Urinary 3-phenoxybenzoic acid (in research studies)	- Supportive care - Symptomatic - Decontamination
Organo-chlorines E.g. Lindane Endosulfan	GABA blockade: - Tremors - Dizziness - Seizures	- Detectable in blood	- Supportive care - Symptomatic - Decontamination

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<<READ SLIDE.>>

Modified from Table of American Academy of Pediatrics. Committee on Environmental Health. In: Etzel ed. *Pediatric Environmental Health, 2nd Ed.* Elk Grove Village IL, 2003.

Ref:

•Aprea C et al. Analytical method for the determination of urinary 3-phenoxybenzoic acid in subjects occupationally exposed to pyrethroid insecticides, *J Chromatogr B Biomed Sci Appl*, 1997, 695:227.

Pesticides

ACUTE PESTICIDE TOXINDROMES

PESTICIDE	ACUTE SYMPTOMS	DIAGNOSIS	TREATMENT
Chlorophenoxy compounds (e.g. 2,4-D)	Nausea, vomiting, acidosis, myalgia fever, myopathy, neuropathy	Detectable in urine and blood	Decontamination and Urine alkalinization
Bipyridyl compounds paraquat	Vomiting Corrosive lesions Hepatotoxicity Acute tubular necrosis Pulmonary fibrosis	Dithionite test in urine	Decontamination Avoid O ₂ haemoperfusion Possibly: corticosteroids and cyclophosphamide
Anticoagulant rodenticide Warfarin Brodifacoum Diphacinone	Haemorrhage (from vit. K antagonism)	Elevated prothrombin time (PT)	Vitamin K1 (Fitomenadione)

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<<READ SLIDE.>>

Modified from Table of American Academy of Pediatrics. Committee on Environmental Health. In: Etzel R. ed. *Pediatric Environmental Health, 2nd Ed.* Elk Grove Village IL, 2003.

LOW-LEVEL CHRONIC EXPOSURE

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

- ❖ Abnormal growth and development
- ❖ Impaired neurobehavioral development / functions
- ❖ 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 additional slides.

Ref:

- *Children in the New Millennium: Environmental Impact on Health*. UNEP, UNICEF, WHO, 2002.
- Eskenazi B et al, Exposures of children to organophosphate pesticides and their potential adverse health effects. *Environ Health Perspect*, 1999, 107(3):409–419.

Pesticides

PRECONCEPTIONAL PRENATAL EXPOSURE

Pesticide exposure before or during pregnancy has been associated with increased risk of:

- Infertility
- Perinatal death
- Spontaneous abortion
- Premature birth
- Fetal growth retardation
- Congenital malformations
- Early childhood cancer



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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:

- Bell EM et al. A case-control study of pesticides and fetal death due to congenital anomalies. *Epidemiology*, 2001, 12:148.
- Berkowitz GS et al. *In utero* pesticide exposure, maternal paraoxonase activity, and head circumference. *Environ Health Perspect*, 2004, 112:388.
- Eskenazi B et al. Association of *in utero* organophosphate pesticide exposure and fetal growth and length of gestation in an agricultural population, *Environ Health Perspectives*, 2004, 112 (10): 1116-1124.
- Garcia AM et al. Parental agricultural work and selected congenital malformations. *Am J Epidemiol* 1999, 149:64.
- Heeren GA et al. Agricultural chemical exposures and birth defects in the Eastern Cape Province, South Africa. A case - control study. *Environ Health*, 2003, 2:11.
- Nurminen T. Maternal pesticide exposure and pregnancy outcome. *J Occup Environ Med*, 1995, 37:935.
- Rojas A et al. Malformaciones Congenitas y exposicion a pesticidas. *Rev Med Chilena*, 2000, 128:399.
- Schreinemachers DM. Birth malformations and other adverse perinatal outcomes in four U.S. Wheat-producing states. *Environ Health Perspect*, 2003, 111 :1259.
- Weidner IS et al. Cryptorchidism and hypospadias in sons of gardeners and farmers. *Environ Health Perspect*, 1998, 106:793.
- Whyatt RM et al. Prenatal insecticide exposures birth weight and length among an urban minority cohort. *Environ Health Perspect*, 2004, 112:1125.

PRENATAL EXPOSURE AND NEURODEVELOPMENTAL EFFECTS

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

- Brain structure and function
- Neuronal and axonal differentiation
- Serotonergic 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 serotonergic system; and
- altered synaptogenesis and programming of synaptic function.

Ref:

•Slotkin TA. Guidelines for developmental neurotoxicity and their impact on organophosphate pesticides: a personal view from an academic perspective, *Neurotoxicology*, 2004, 25:631.

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.

PRENATAL EXPOSURE AND NEURODEVELOPMENTAL EFFECTS

**Mechanisms of developmental toxicity may be
different from those of acute toxicity**

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 RNA 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:

- Aldridge JE et al. Serotonergic systems targeted by developmental exposure to chlorpyrifos: effects during critical periods. *Environ Health Perspect*, 2003, 111:1736.
- Colosio C et al. Neurobehavioral effects of pesticides. State of the art. *Neurotoxicology*, 2003, 24:577.

CHRONIC NEUROLOGICAL EFFECTS

- ❖ Neurological sequelae of acute poisoning
- ❖ Neurological symptoms due to high indoor levels of pesticides
- ❖ Subtle changes in memory and attention

It may be difficult to differentiate the effects of prenatal exposure from 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.

Refs:

- American Academy of Pediatrics Committee on Environmental Health. Pesticides. Chapter 24. In: Etzel R. ed. *Pediatric Environmental Health 2nd Ed* Elk Grove Village IL, American Academy of Pediatrics, 2003.
- Eskenazi B et al, Exposures of children to organophosphate pesticides and their potential adverse health effects. *Environ Health Perspect*, 1999, 107(3):409–419.
- Keifer M et al. Symptoms and cholinesterase activity among rural residents living near cotton fields in Nicaragua. *Occup Environ Med*, 1996, 53:726.
- Ruckart PZ et al. Long-term neurobehavioral health effects of methyl parathion exposure in children in Mississippi and Ohio. *Environ Health Perspect*, 2004, 112:46.
- Wagner SL et al. Chronic organophosphate exposure associated with transient hypertonia in an infant. *Pediatrics*, 1994, 94:94.

PESTICIDES AND CHILDHOOD CANCER

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

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

A number of epidemiologic 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:

- Borkhardt A et al. Congenital leukaemia after heavy abuse of permethrin during pregnancy. *Arch Dis Child Fetal Neonatal Ed.* 2003, 88:F436.
- Daniels JL et al. Residential pesticide exposure and neuroblastoma. *Epidemiology*, 2001. 12:20.
- Leiss JK et al. Home pesticide use and childhood cancer: a case-control study. *Am J Public Health*, 1995, 85:249.
- Ma X et al. Critical windows of exposure to household pesticides and risk of childhood leukaemia. *Environ Health Perspect*, 2002, 110:955.
- Pogoda JM et al. Household pesticides and risk of pediatric brain tumors. *Environ Health Perspect*, 1997, 105:1214.

PRENATAL EXPOSURE AND CHILDHOOD CANCER

- ❖ Maternal exposure to pesticide has been associated with paediatric cancer – acute lymphocytic leukaemia

- ❖ Association with parental occupational exposure
 - Leukaemia
 - Brain cancer
 - Hodgkin and non-Hodgkin lymphomas
 - Kidney cancer

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:

- Efrid JT et al. Farm-related exposures and childhood brain tumours in seven countries: results from the SEARCH International Brain Tumour Study. *Paediatr Perinat Epidemiol*, 2003, 17:201.
- Flower KB et al. Cancer risk and parental pesticide application in children of agricultural health study participants. *Environ Health Perspect*, 2004, 112:631.
- Infante-Rivard C et al. Risk of childhood leukemia associated with exposure to pesticides and with gene polymorphisms. *Epidemiology*, 1999, 10:481.
- Rodvall Y et al. Cancer risk in offspring of male pesticide applicators in agriculture in Sweden. *Occup Environ Med*, 2003, 60:798.
- Zahm SH et al. Pesticides and childhood cancer. *Environ Health Perspect*, 1998, 106:893.

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
- ❖ Endocrine disruption has been linked to:
 - 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, vinclozilin, procymidone)
- anti-thyroid effects (ethylenethiourea (ETU), maneb, zineb metabolites)
- anti-progestin effects (DDT).

Synthetic pesticides may interfere with the natural process of development.

Refs:

- Baskin LS et al. Hypospadias and endocrine disruption, is there a connection? *Environ Health Perspect*, 2001, 109:1175.
- Damstra T et al. *Global assessment on the state of the science of endocrine disruptors*. IPCS. UNEP/ILO/WHO, 2002.
- Gray LE et al. Effects of environmental antiandrogens on reproductive development in experimental animals. *Hum Reprod Update*, 2001, 7:248.
- Landrigan P et al. Assessing the effects of endocrine disruptors in the National Children's Study. *Environ Health Perspect*, 2003, 111:1678.

IMMUNOTOXICITY

❖ **Immunotoxicity is suspected, but evidence is limited**

Studies in Arctic zone:

- Higher incidence of ear infections
- Cytokine panel abnormalities



www.smithsonianmag.si.edu/smithsonian/issues04/jan04/images/topdogs_mush_jpg.html

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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.

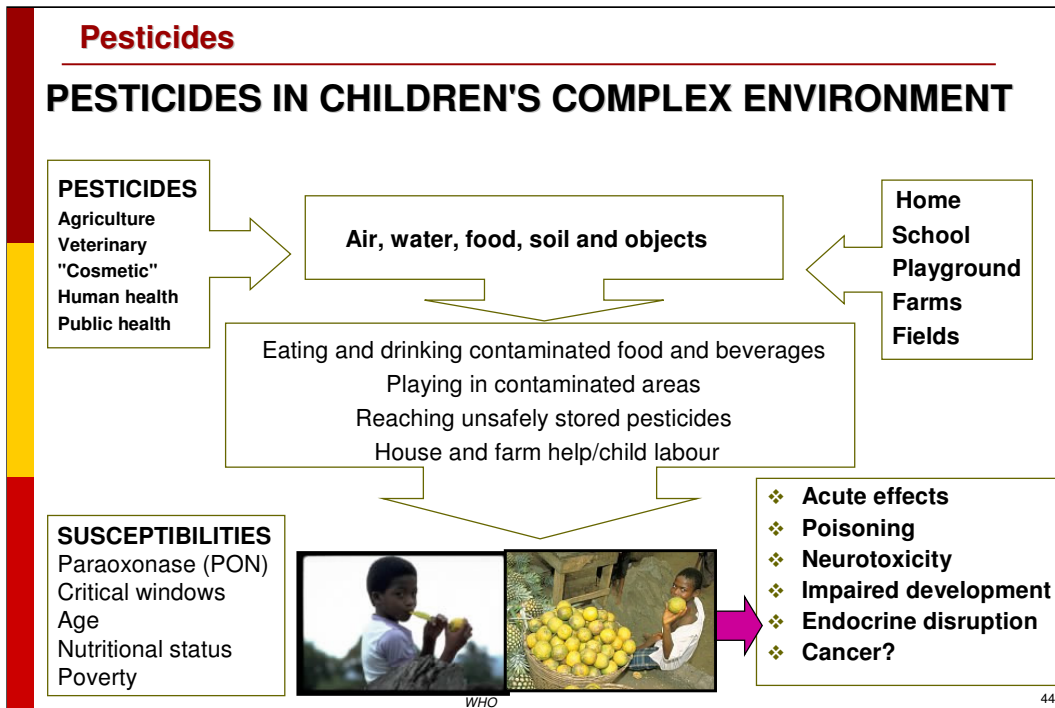
Inuit infants from the Arctic exposed *in utero* and to breast milk contaminated with *p,p'*-DDE, hexachlorobenzene and dieldrin had an elevated risk of otitis media.

Refs:

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- Duramad P et al, Expression of Th1/Th2 cytokines in human blood after in vitro treatment with chlorpyrifos, and its metabolites, in combination with endotoxin LPS and allergen Der p1, *J Appl Toxicol*, 2006, 26(5): 458-65.
- Phillips TM. Assessing environmental exposure in children: immunotoxicology screening. *J Exp Anal Environ Epidemiol*, 2000, 10:769.

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 ("cosmetic"), 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
- helping in the house and on the farm or as child labour
- Contact with clothing or shoes of working parents

Children have special susceptibilities related to:

- paraoxonase (PON) - it catalyzes the hydrolysis of toxic metabolites and can protect against pesticide toxicity, which then depends on the PON genotypes
- critical windows of susceptibility
- age
- nutritional status
- 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
- 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 right: WHO, P. Viot. Fruits and vegetables, Ghana, 2003

Picture on the left: WHO, C. Gaggero. Jamaica, Nutrition and child

Pesticides

OBSOLETE PESTICIDES

Obsolete pesticides are pesticides that can no longer be used for their intended purpose or any other purpose.

They may include:

- ❖ Pesticides in liquid, powder or dust, granule, emulsion form.
- ❖ Empty and contaminated pesticide containers
- ❖ Heavily contaminated soil
- ❖ Buried pesticides

Causes of obsolete pesticides:

- ❖ Use prohibited for health/environmental reasons
- ❖ Product deteriorated as result of improper or prolonged storage
- ❖ Product not suitable for intended use and cannot be used for other purposes, nor can it easily be modified to become usable.

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Obsolete, unwanted and banned pesticides are serious environmental hazards. Leaking and corroding metal drums filled with obsolete and dangerous pesticides dot urban and rural landscapes of developing countries around the world. These chemical leftovers have become villains in the agricultural world they were designed to help, affecting not only a nation's agriculture and its environment, but also fundamentally the health of its people and consequently development in general be it in rural areas or under urban conditions.

This global environmental tragedy is a direct result of several decades of mishandling and misuse, but is most dramatic in the developing world where there is no awareness of the inherent danger of pesticides. The unaware therefore draw water from contaminated site for own survival and that of their animals.

Obsolete pesticides may include: <<READ SLIDE>>

Most of the affected countries are under tropical conditions where agricultural and vector pests flourish both in diversity and numbers. Migratory pests such as locusts, grasshoppers, grain eating birds, storage pests, rodents, etc. inflict untold damage to agriculture and bring about hunger or misery when they are at their peak.

Poor nations have been led to believe that the only alternative to combat pests agricultural or otherwise effectively is only by using pesticides. The poor or the unaware never think for a moment that pesticides are poisonous and that they are dangerous to life. Most believe that pesticides are like medicines. They consider that they kill pests selectively and are therefore less harmful to humans, animals and plants. Governments save budgets to purchase pesticides on regular basis. Also constantly plead to donors and organizations for assistance either for direct supply of pesticides or for contributions of financial support for purchasing them. In response, donors and organizations supply pesticides.

Recipient countries anxious to minimize pest damages to the minimum or, being less aware of the negative consequences, usually receive pesticides from every possible source and direction. This leads to uncoordinated influx of pesticide donations and trading, subsequently giving rise to excessive supply. While some of the donations are genuine, others take the opportunity to dump unwanted and illegal pesticides on the poor and unsuspecting countries. Pesticides reach individual farmers or household dwellers that value pesticides dearly. They keep them in their houses, with their food and animals. Pesticide vendors take the opportunity to promote pesticides aggressively. It is not uncommon to find pesticides being stored in the open or in heavily populated zones and usually in substandard stores and sold along with food and drinks, etc. Children are used in advertising sales of pesticides and often get easy access to pesticides.

They play with empty pesticide cans and use them for drinking water or milk. Most pesticide cans litter high streets or are simply dumped in open municipality dumps for subsequent open burning leading to serious emissions of dioxins.

Common causes of obsolete pesticides include the following:

- Use of the product has been prohibited or severely restricted for health or environmental reasons (e.g. through banning; withdrawal of registration, or policy decision by relevant government agencies)
- The product has deteriorated as a result of improper or prolonged storage and can no longer be used according to its label specifications and instructions for use, nor can it easily be reformulated to become usable again.
- The product is not suitable for its intended use and cannot be used for other purposes, nor can it easily be modified to become usable.

Other possible reasons for why we have obsolete pesticide include:

- Banning of pesticides that are still kept in store.
- Aggressive pesticide sales, promotions and distributions by the Chemical Industry.
- Difficulties in forecasting outbreaks of pest.
- Inappropriate assessment of pesticide requirements.
- Insufficient application capacity.
- Inappropriate formulations or substandard containers.
- Excessive donations: these are usually inappropriate because they are not received when needed most (i.e. late arrival of donations or out of season delivery), or are uncoordinated with similar donations from various sources. Such are tantamount to dumping.
- Inadequate storage facilities and lack of staff trained in storage management (i.e. poor stock taking and lack of records).
- Ineffective distribution or poor marketing systems for pesticides (government or private sector or both).
- Lack of awareness of the inherent dangers of pesticides.
- Misuse of pesticide containers (e.g. for a variety of domestic uses, water containers, food storage, use for pot plants, etc.).

Notes from FAO: www.fao.org/WAICENT/FAOINFO/AGRICULT/AGP/AGPP/Pesticid/Disposal/index_en.htm

OBSOLETE PESTICIDES

Disposal of obsolete pesticides:

- ❖ United Nations Food and Agriculture Organization has developed a set of guidelines for disposal.
- ❖ Contact your local authorities for advice on disposal.



FAO

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Disposal of obsolete pesticides:

- In many countries, obsolete pesticides are a problem. The United Nations Food and Agriculture Organization have developed a set of guidelines for disposal, available at: www.fao.org/WAICENT/FAOINFO/AGRICULT/AGP/AGPP/Pesticid/Disposal/index_en.htm.
- Contact your local authorities for advice on disposal.

WHO Recommended Classification by Hazard contains a table of active ingredients (available at: www.inchem.org/documents/pds/pdsother/class.pdf) believed to be obsolete or discontinued for use as pesticides.

<< NOTE TO USER: Do you have stockpiles of obsolete pesticides in this country? If so, what is the reason for it?>>

Notes from FAO:

www.fao.org/WAICENT/FAOINFO/AGRICULT/AGP/AGPP/Pesticid/Disposal/index_en.htm

Picture: FAO, I. Balderi. Obsolete pesticides that have heavily leaked into the environment polluted and contaminated ground water and containers left from domestic use have disappeared into the soil.

Pesticides

PREVENTION OF EXPOSURE

What can be done to prevent pesticide exposure and poisoning ?

❖ Take action at

- Local level
- National level
- International



WHO

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<<READ SLIDE.>>

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

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

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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).

Refs:

- UNEP Chemicals. *Childhood Pesticides Poisoning. Information for Advocacy and Action. May 2004* (www.who.int/ceh/publications/en/pestpoisoning.pdf).
- US EPA Webpage for Integrated Pest Management (www.epa.gov/pesticides/food/ipm.htm).

Pesticides

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



WHO

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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"
- support for organic farming

FAO: Food and Agriculture Organization

<<READ SLIDE.>>

Picture: WHO, P. Virof. Plants at the Biofarm, Ethiopia, June 2002.

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 Environmental Protection Agency 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.

Refs:

- UNEP Chemicals. *Childhood Pesticides Poisoning. Information for Advocacy and Action. May 2004* (www.who.int/ceh/publications/en/pestpoisoning.pdf).
- US EPA Website Food Quality Protection Act, 1996 (www.epa.gov/oppfead1/fqpa/backgrnd.htm).

Pesticides

PREVENTION – INTERNATIONAL LEVEL

- ❖ **Persistent organic pollutants (POPs)**
Stockholm Convention
- ❖ **Hazardous chemicals and pesticides**
Rotterdam Convention (PIC)
- ❖ **International organizations:**
WHO, IFCS, FAO, ILO



Pronczuk

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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.

IFCS: Intergovernmental Forum for Chemical Safety

FAO: Food and Agriculture Organization

ILO: International Labour Organization

Refs:

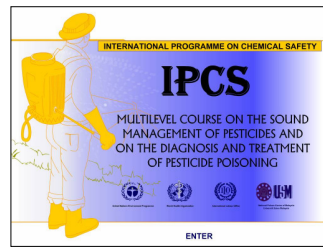
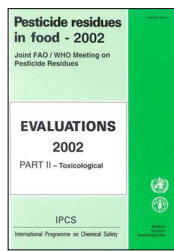
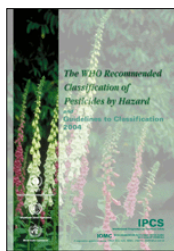
•UNEP Chemicals. *Childhood Pesticides Poisoning. Information for Advocacy and Action. May 2004* (www.who.int/ceh/publications/en/pestpoisoning.pdf).

•www.pic.int

Pesticides

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. Training manual on pesticides
5. Poison centres and pesticide exposures



WHO

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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

3. International pesticide limits in water. WHO produces international norms on water and health in the form of guidelines.

Ref: www.who.int/water_sanitation_health/dwq/guidelines/en/

4. Training manual on pesticides. 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/

IPCS: Intergovernmental Programme on Chemical Safety

FAO: Food and Agriculture Organization

Pictures: WHO

CRITICAL ROLE OF HEALTH AND ENVIRONMENT PROFESSIONALS



WHO

- ❖ Diagnose and treat
- ❖ Publish, research
 - Sentinel cases
 - Community-based interventions
- ❖ Educate
 - Patients and families
 - Colleagues and students
- ❖ Advocate
- ❖ Provide role model

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.

POINTS FOR DISCUSSION

<<NOTE TO USER: Add points for discussion according to the needs of your audience.>>

CASE STUDY

- ❖ A family with two children ages 8 months and 6 years are referred to the clinic with concerns of pesticide exposure.
- ❖ They are worried because their apartment was sprayed with pesticides for termites 3 times when the mother was pregnant with her 6 year old son. She remembers feeling dizzy and fatigued during that period but attributed it to the pregnancy.

<<READ SLIDE>>

The setting is present day New York City, United States. This family is poor and lives in low income housing that was likely sprayed multiple times for termites. The most commonly used pesticide at that time was chlorpyrifos.

CASE STUDY

- ❖ Her six year old was born at low birth weight for gestational age and has been behind in meeting developmental milestones. He now has behavioural problems and is behind in reading in school.
- ❖ She recently read in the newspaper that chlorpyrifos is not being used in residential settings in the US because it stays on surfaces for long periods of time and may have harmful health effects.

Read the Slide

The mother was told by someone at work that there was a newspaper article on a pesticide (chlorpyrifos) that was widely used in their part of New York. It stated that the the US Environmental Protection Agency phased out its use because of adverse health effects. The article pointed out that mothers who were exposed to chlorpyrifos prenatally may have delivered low birth weight babies.

Pesticides

CASE STUDY

- ❖ She is wondering if her son's low birth weight and difficulties in school could be due to chlorpyrifos exposure.
- ❖ She asks if she should be worried about her 8 month old being exposed given that chlorpyrifos can stay on surfaces for long periods of time.

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As we know, pediatricians treat the entire family not just individual children. This case brings up a number of interesting points regarding each family member.

Pre-Test

1. What are the problems lists for the 6 year old and 8 month old?
2. What differential diagnoses would you consider for the 6 year old?
3. What further history do you want?
4. How would you further evaluate and manage these patients?
5. What is the likelihood that prenatal chlorpyrifos exposure is related to the 6 year old's health problems?

Pesticides

BACKGROUND

- ❖ **Chlorpyrifos (Dursban/Lorsban) is an organophosphate chemical. It acts as a pesticide by interfering with the acetylcholinesterase enzyme necessary for normal neurological functioning.**

- ❖ **It was used for the following purposes:**
 - agriculture indoor crack/crevice sealant
 - pet collars treatment for lawns/turf
 - cattle ear tag indoor termiticide
 - mosquitocide

- ❖ **An estimated 20-24 million pounds of chlorpyrifos were applied annually in the late 1990s. 50% for agricultural use and 50% non-agricultural purposes.**

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Chlorpyrifos is in the organophosphate family of chemicals. It is a known human toxin that persists in the environment for decades. Chlorpyrifos is released into the environment and can travel through waterways and sediments to enter the food supply by way of farming or the fish/animal supply. It is ubiquitous in all parts of the world.

It has been used in farming extensively as a pesticide thereby exposing numerous food crops to its residues.

It has been used as an insecticide for termites and mosquitoes. It has been used as an indoor crack/crevice sealant, for pet collars, and as treatment on lawns, turf or pastures.

US EPA estimates that 20-24 million pounds of chlorpyrifos were applied annually in the late 1990s. Mitigation measures were put into place in the US in 2000 to phase out uses near or in schools, homes, parks, and daycare centers and to restrict uses in agricultural settings.

Ref:

US EPA Website Organophosphate Pesticide Information

Pesticides

CASE STUDY

- ❖ **Apartment was sprayed with chlorpyrifos 3 times during pregnancy with 6 yr old son. She was dizzy and fatigued surrounding the times of spraying.**
- ❖ **She is wondering if her six year old son's low birth weight and difficulties in school could be due to the chlorpyrifos exposure.**
- ❖ **She asks if she should be worried about her 8 month old being exposed given that chlorpyrifos can stay on surfaces for long periods of time.**

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Now, let's go back to the original case.

What does this information tell you and what more do you want to know?

1. First, this mother was exposed when she was pregnant. We would like to know the exact chemicals used and have documentation of the exposure. Also, we need to take a thorough environmental history:
 - Exposures to other environmental toxicants (there may be other substances in the household contributing to her health effects during pregnancy)
 - What are the occupations of the parents? Are there potential environmental exposures at work?
 - When is/was the exposure? Is it continuing currently?
 - What are the main effects? We would like to know more about the mother's symptoms during pregnancy (although there does not need to be overt clinical symptoms for low level toxicity).
2. In terms of the six year old son – we would like to know his birth weight, length, and head circumference
 - How has his growth has been?
 - What is his developmental history?
 - What are his activities and what he might be exposed to in the environment?
3. In terms of the 8 month old, we would like to know if he is crawling currently (exposure to floor, carpets, furniture).
 - Is he still breastfeeding?
 - How has his development been?

ANSWERS

Overall, there are not clear cut answers in low dose exposure toxicology as compared to acute exposures. All answers must weigh the scientific evidence of the toxicant against the clinical history and physical exam findings of the patients.

1. Chlorpyrifos exposure in high doses is associated with dizziness and fatigue. The differential diagnosis for her symptoms is long and, it is difficult say whether the mother's symptoms were due to this exposure given that most residential chlorpyrifos sprayings were not associated with overt toxicity.
2. Her son's low birth weight and difficulties in school may be due to a number of factors. Chlorpyrifos has been associated with low birth weight and decreased birth length in inner city newborns whose mothers were exposed during pregnancy. Long term neurodevelopmental outcomes have not been studied to date.
3. The 8 month old is crawling and being exposed to many surfaces in the home. The data has shown that higher levels of chlorpyrifos are inversely correlated with time from application to testing. Most of this data shows that residues persist for 1-2 wks after spraying but with multiple exposures, residues may persist longer.

CASE STUDY

What recommendations would you give to this family?

- ❖ **Primary prevention!**
- ❖ **Encourage home dust/furniture testing if they think exposure is ongoing**
- ❖ **Encourage blood testing for acetylcholinesterase if they are worried about ongoing exposures**
- ❖ **Encourage alternatives to pesticides for the future**

Pesticides

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Pesticides

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