

**Training Course on Reproductive Health Research  
13 March 2007, WHO HQ**

---

**ENVIRONMENTAL INFLUENCES  
ON REPRODUCTIVE HEALTH:  
FROM CONCEPTION TO BIRTH...AND BEYOND**



**Children's Health and the Environment  
WHO Training Package for the Health Sector  
World Health Organization  
[www.who.int/ceh](http://www.who.int/ceh)**

## WHAT IS THE ENVIRONMENT?

***"Everything that is not me"***

*A. Einstein*

***"Everything that surrounds anything"***

*web.mala.bc.ca*

All the physical, chemical, biological and social factors that may affect the origin, growth, development and survival of an organism in a given setting.

## WHAT IS FERTILITY?

- ❖ Classically (medical dictionary):
  - Fertility: The ability to conceive and have children, the ability to become pregnant through normal sexual activity.
  - Infertility: failure to conceive after a year of regular intercourse without contraception.
  
- ❖ WHO recommends 24 months of unprotected intercourse as the preferred definition of the condition
  
- ❖ Demographers: infertility as the inability of a noncontracepting, sexually active woman to have a live birth

## Causes and estimated number of deaths/year in children 0 to 4 yrs

|  |                  |
|--|------------------|
| <b>Acute respiratory infections:</b>   | <b>1 000 000</b> |
| <b>Diarrhoeal diseases:</b>            | <b>1 600 000</b> |
| <b>Malaria and other vector-borne:</b> | <b>1 000 000</b> |
| <b>Injuries (non-intentional)</b>      | <b>300 000</b>   |
| <b>Poisonings</b>                      | <b>16 000</b>    |

*www.who.int/evidence 2002 data*

*The environment and health for children and their mothers, Fact sheet WHO/284, 2005*

**Diseases strongly linked to environmental threats are present in places where children grow, live, learn and... work**

**WHO ACTIVITIES ON CHILDREN'S HEALTH & THE ENVIRONMENT**

## **MAIN GLOBAL ENVIRONMENTAL HEALTH RISKS**

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

**Over 5 000 000 children under 14 yrs die every year from diseases that relate to environmental conditions, mainly in the developing world.**

The biological process of reproduction involves:

- **Production of healthy germ cells**
- **Conception**
- **Viable conceptus (embryo)**
- **Growth & development of fetus in favourable maternal environment**
- **Successful delivery of baby**
- **Growth and development of baby into healthy child and a healthy adult ... and parent!**

*Any environmental factor that affects one or more of these key stages can result in reproductive failure*

# REPRODUCTIVE HEALTH

❖ **Females are born with all their ova**

Exposure to toxicants during the formation of fetal ovaries and ova will impact on future generations.

❖ **Males produce sperm continuously**

Past, recent, or ongoing occupational/environmental exposures may alter spermatogenesis – with possibility of "recovery"

*E.g.: Lead and some pesticides have been detected in follicular fluid and semen*

# REPRODUCTIVE TOXICANTS/FACTORS

## ❖ Effects on the female reproductive system:

- Sexual behaviour
- Onset of puberty and menstrual cycles
- Fertility (decreased)
- Gestation time
- Lactation (decreased)
- Menopause (cause premature menopause)

*Eg: - Lead exposure: menstrual disorders, infertility  
- PCBs can bring irregularities in menstrual cycle.*



## ENVIRONMENTAL THREATS TO FEMALE FERTILITY

### Causes of female infertility:

- Tubal factors 36%
- Ovulatory factors 33%
- Endometriosis 6%
- Unknown 40% ?? ← *Environmental?*

### *Examples:*

- *Car exhaust fumes: reduction in ovarian weight, n° follicles*
- *Coffee linked to higher risk of not conceiving for 12 months*
- *Smoking and obesity linked to ageing of genetic material*
- *Traces of DDE, mirex, PCBs found in follicular fluid*

# REPRODUCTIVE HEALTH

## DES (diethylstilbestrol)

**Synthetic hormone developed in 1930s to prevent miscarriage, administered to 10 million women**

**Mothers who took DES:**

- ❖ **Daughters: clear-cell vaginal adenocarcinoma, uterus abnormalities, difficulty to conceive**
- ❖ **Boys: epididymal cysts, hypospadias, cryptorchidism**
- ❖ **Higher rates of breast cancer**

# MOTHERS AND THEIR OFFSPRING

## Pre-conception

PCBs and Pb maternal body burdens are linked to abortion, stillbirth and learning disabilities  
Folate deficiency leads to neural tube defects

## *In utero*

|                |   |                              |
|----------------|---|------------------------------|
| Thalidomide    | → | phocomelia                   |
| DES            | → | vaginal cancer               |
| X-rays         | → | leukaemia                    |
| Heat           | → | neural tube defects          |
| Alcohol        | → | FAS (Fetal Alcohol Syndrome) |
| Lead           | ↗ | Neurodevelopmental effects   |
| Methyl mercury | ↗ |                              |
| PCBs           |   |                              |

# REPRODUCTIVE TOXICANTS/FACTORS

## ❖ Effects on male reproductive system:

- Sperm count and morphology
- Sexual behaviour
- Fertility (decreased)

## *Eg:*

- *Phtalates, PCBs and organochlorine pesticides: sperm quality*
- *Lead: reduces male fertility*
- *Carbon disulfide*
- *Pesticides (chlordecone, dibromochloropropane)*
- *Scrotal hyperthermia*

## **Environmental factors that influence fertility:**

### **DBCP (dibromo-3-chloropropane)**

#### **Pesticide used in banana & pineapple plantations**

- **Azoospermia and oligospermia in 64 to 90% of men exposed for 3 ys**
- **Failure of spermatogonial development (rats)**
- **DBCP-treated human sperm does not penetrate the oocytes**

***Given the persistent nature of DBCP contamination in areas of past use, efforts should be made to remediate these areas and to follow exposed populations for development of certain human cancers, including breast, ovarian, stomach, respiratory, oral and nasal cancers, among others.***

*Clark & Snedeker - Critical evaluation of the cancer risk of bromochloropropane  
Environ Sci Health C Environ Carcinog Ecotoxicol Rev. 2005;23(2):215-60.*

## ENVIRONMENTAL THREATS TO MALE FERTILITY

- ✓ **Smoking**
- ✓ **Pesticides**
- ✓ **POPs (PCBs, dioxins)**
- ✓ **Solvents**
- ✓ **Air pollution**
- ✓ **Monosodium glutamate** (*flavour enhancer: chips, soups, ....*)
- ✓ **Obesity**
- ✓ **Anaesthesia** (*enflurane*)
- ✓ **Soya products** (*affects ability of sperm to enter the egg*)
- ✓ **Cocaine**
- ✓ **Chlorine-based chemicals (suspected)**
- ✓ **High scrotal temperature (laptop users)** *Sheynkin ,Y. et al, Hum Reprod., 20 (2) 452-5, 2005.*

## **FATHERS AND THEIR OFFSPRING**

- ❖ **Paternal exposure to:** Hg, ethylene oxide, rubber chemicals, solvents,  
linked to spontaneous abortion
- ❖ **Paternal occupation:**
  - Painters – anencephaly**  
(Brender. *Am J Epidemiol*, 1990, 131(3):517)
  - Mechanics, welders – Wilms tumour**  
(Olshan. *Cancer Res*, 1990, 50(11):3212)
  - Textiles – stillbirth, pre-term delivery**  
(Savitz. *Am J Epidemiol*, 1989, 129(6):1201)

**Possible mechanism: impairment of a paternal gene required for the normal growth and development of the fetus**

***“The special and unique vulnerability of children to environmental hazards”*** *Bearer, Neurotoxicology, 2000, 21(6):925*

# REPRODUCTIVE TOXICANTS

## POPs (Persistent Organic Pollutants) *Stockholm Convention*

- **CB-153 and DDE in semen of 149 Swedish fishermen (Baltic Sea) with a high proportion of Y-chromosome bearing semen. Also high levels of the POPs in blood.**
- **Higher prevalence of chryptorchidism in Lithuania**

***Environmental factors may be changing the ratio of sperm carrying the X or Y (sex determining) chromosomes and may be contributing to male reproductive disorders***



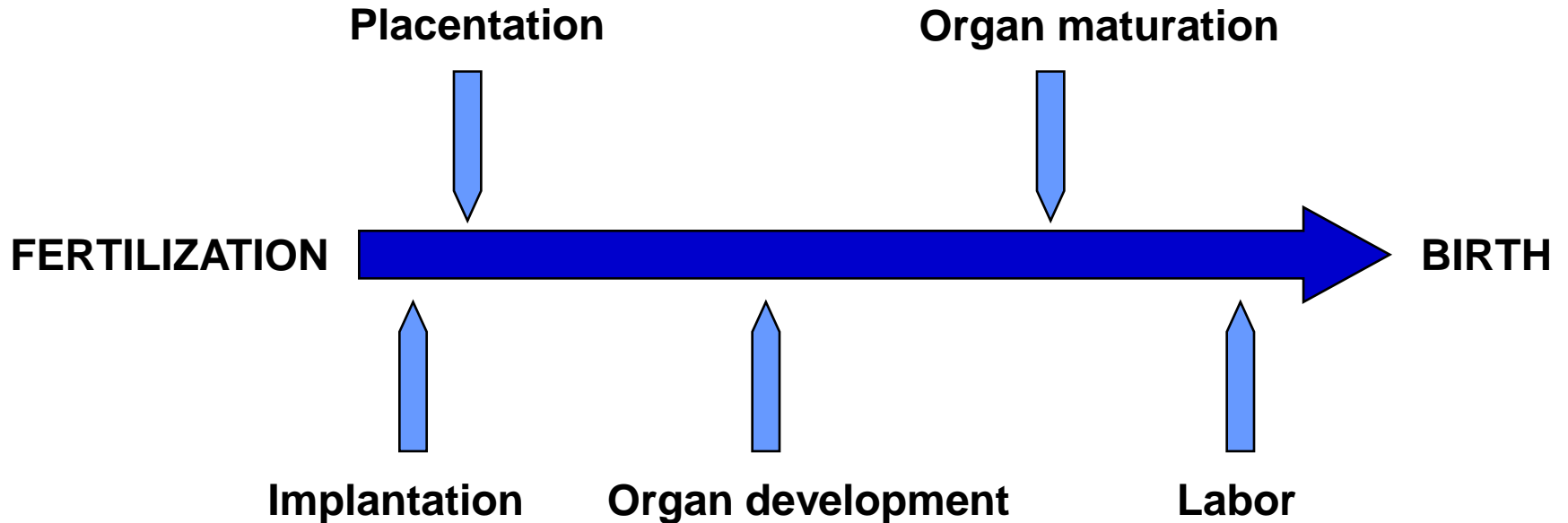
## **REPRODUCTIVE HEALTH**

**Adverse occupational and environmental exposures may result in adverse reproductive outcomes:**

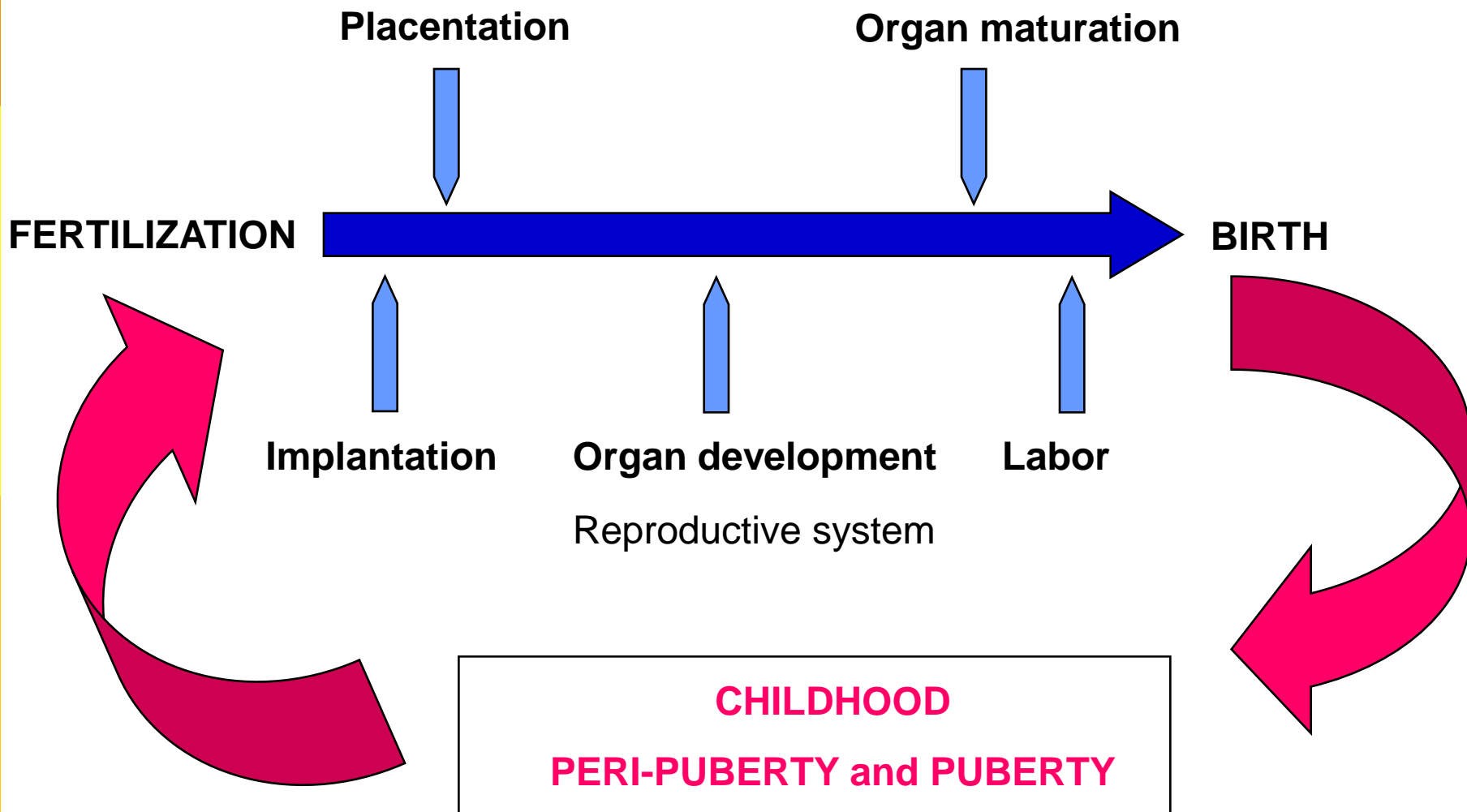
- **Reduced semen quality**
- **Ovarian dysfunction**
- **Infertility**
- **Fetal loss**
- **Growth retardation**
- **Altered parturition**
- **Still birth and birth defects**

***Timing of exposure is crucial!***

## Environmental factors influence:



## Environmental factors influence:



## **CRITICAL WINDOWS OF EXPOSURE IN REPRODUCTIVE HEALTH**

- **Pre-conceptual**
- **Pre-natal**
  - **Gonadal differentiation**
  - **Urogenital system development**
  - **Breast development**
- **Early post-natal**
- **Peripuberty and puberty**

## **CRITICAL WINDOWS OF EXPOSURE IN REPRODUCTIVE HEALTH**

### **Pre-conceptual**

- **Damage to spermatozoal DNA may result in embryo death or fetal malformations**
- **Numerical errors or structural changes in sex chromosomes: abnormal gonadal development and infertility (e.g. deletion in the Y chromosome)**

## CRITICAL WINDOWS OF EXPOSURE IN REPRODUCTIVE HEALTH

### Pre-natal

- **Gonadal differentiation**

- Migration and proliferation of germ cells to form the gonad
- Proliferation to establish a pool of oogonia or spermatogonia

- **Urogenital system development**

- Regulated by hormonal systems
- POPs and hypospadias? Cryptorchidism? Testicular maldescent?
- DES – effects that appeared after puberty
- Progesterone and hypospadias

- **Breast development**

## Environmental risk factors and pre-term delivery

- **Occupational exposures** (solvents in W; pesticides in M)
- **Air pollutants**
- **POPs**
- **DDE (metabolite of DDT)**
- **Ethane**
- **PCBs – affects growth of female fetus**
- **Metals: Pb, As**
- **Water disinfection by-products**
- **Video display terminals**

## Environmental risk factors and pre-term delivery

### Air pollutants

- **Maternal smoking: 2-fold increase in LBW and IUGR**
- **Second-hand tobacco smoke and LBW**

*Tobacco smoke causes chronic hypoxia: lowers maternal uterine blood flow, reduces supply of O<sub>2</sub> from uterus to placenta, raises maternal and fetal COHb levels*

- **PM 10 or PM2.5 linked to LBW or IUGR**
- **CO**
- **SO<sub>2</sub>**
- **Polycyclic aromatic hydrocarbons (PAH)**



## **CRITICAL WINDOWS OF EXPOSURE IN REPRODUCTIVE HEALTH**

### **Early post-natal**

- **First 6 months crucial for testis development**
- **Exposure to PCB and anti-thyroid activity**

### **Peripuberty and puberty**

- **Developing testes are more sensitive (phthalate esters; DBCP; dinitrobenzene...)**
- **Ovarian toxicants poorly characterized – depletion of oocytes associated with early menopause, osteoporosis, ...**

## **Environmental factors influence:**

- **Conception (and pre-conception)**
- **Pregnancy**
- **Embryo/fetus**
- **Child birth**
- **Newborn/infant/child/adolescent (and adults!)**

***With an effect on: HEALTH  
DEVELOPMENT  
WELL BEING***

## ADVICE ON HOW TO REDUCE EXPOSURE TO CHEMICALS

- ✓ *Eat fewer processed foods (which contain additives)*
- ✓ *Eat organic food (without pesticides and preservatives)*
- ✓ *Eat seafood low in PCB and mercury contamination (salmon, canned tuna)*
- ✓ *Don't microwave in plastic containers*
- ✓ *Use a home filter for tap water.*
- ✓ *Eat less meat and high fat dairy products*
- ✓ *Use less cosmetics and personal care products*
- ✓ *Avoid artificial fragrances*
- ✓ *Don't use solvents and stain repellents*
- ✓ *Reduce number of household cleaners (use soap and water!)*
- ✓ *Do not use gasoline-powdered yard tools (only manual or electric)*
- ✓ *Avoid breathing gasoline fumes when filling your car*

## **IF PREGNANT ALSO**

- ✓ *Don't smoke, no alcohol, no caffeine, no extreme body weight*
- ✓ *Ask someone else to use cleaners and pump gas for you.*
- ✓ *Paint baby room long before you conceive or have it done*
- ✓ *Don't use nail polish, solvents, ...*
- ✓ *Eat canned salmon instead of canned tuna.*
- ✓ *Don't allow smoking in your household*
- ✓ *Calcium supplements minimize mineral loss, reducing the release of lead fixed in the bones (associated to calcium)*

## IF PREGNANT ALSO

***Many pregnancy/birth problems could be avoided through:***

- **Family planning,**
- **Balanced, organic diet**
- **Management of maternal health problems**
- **Avoiding maternal infection**

**Usual advice:**

- ✓ ***Folic acid in flour to prevent neural tube defects,***
- ✓ ***Iodine in salt to prevent congenital hypothyroidism,***
- ✓ ***Vit B12 (methyl donor important for DNA and protein modification) around conception***
- ✓ ***Rubella vaccinations prevents congenital rubella syndrome.***

## **RECOMMENDATIONS TO WORKING PARENTS**

- ✓ ***Recognize teratogens and learn about them.***
- ✓ ***Ask for policies and procedures that protect reproductive health in your workplace***
- ✓ ***Do not rely only on material safety data sheets and ask for specific information***
- ✓ ***Request the replacement of potential teratogenic agents with safer materials.***
- ✓ ***Be cautious and make informed choices***

## Environment and reproductive health

---



WHO

*"Improving children and mothers' (and fathers') environmental health by addressing and tackling issues affecting their health, presents an essential contribution towards the achievement of the Millennium Development Goals (MDGs)"*

<http://www.who.int/ceh/publications/factsheets/fs284/en/>