Training Course in Reproductive Health / Sexual Health Research
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ENVIRONMENTAL INFLUENCES ON REPRODUCTIVE HEALTH: FROM CONCEPTION TO BIRTH…AND BEYOND

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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.

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

Acute respiratory infections:	**1 000 000**
Diarrhoeal diseases:	**1 600 000**
Malaria and other vector-borne:	**1 000 000**
Injuries (non-intentional)	**300 000**
Poisonings	**16 000**

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.

www.who.int/world-health-day/2003

Environment and reproductive health

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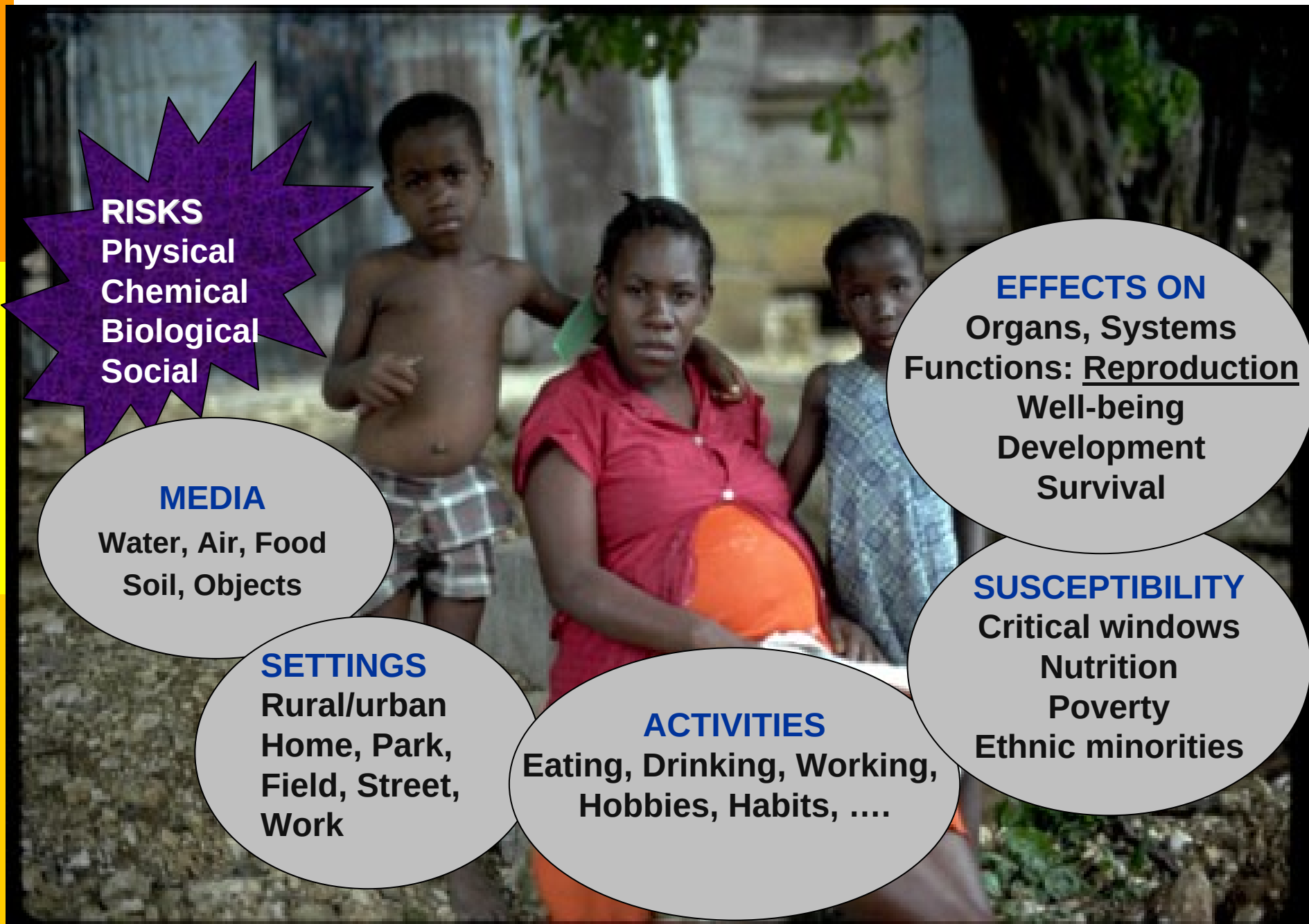



COMPLEX ENVIRONMENTS,
MULTIPLE PROBLEMS,
STRATEGIC APPROACHES
RISKS
Physical
Chemical
Biological
Social
EFFECTS ON
Organs
Systems
Functions
Well-being
Development
Survival
MEDIA
Water, Air, Food
Soil, Objects
SUSCEPTIBILITY
Critical windows
Nutrition
Poverty
Ethnic minorities
SETTINGS
Rural/urban
Home, Park,
Field, Street,
Work
ACTIVITIES
Eating, Drinking, Working,
Hobbies, Habits, ….

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

- **<u>Females</u> are born with all their ova**
  - **Exposure to toxicants during the formation of fetal ovaries and ova will impact on future generations.**

- **<u>Males</u> produce sperm continuously**
  - **Past, recent, or ongoing occupational/environmental exposures may alter spermatogenesis – with the possibility of "recovery"**

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

REPRODUCTIVE TOXICANTS/FACTORS

❖ **Effects on the <u>female</u> 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% ??**

Eg. :

- ***Car exhaust fumes linked to reduction in ovarian weight and n° of follicles***
- ***Coffee linked to higher risk of not conceiving for 12 months***
- ***Smoking and obesity linked to ageing of genetic material***

REPRODUCTIVE HEALTH

DES (diethystilbestrol)

Synthetic hormone developed in 1930s to prevent miscarriage

Mothers who took DES:

- **Daughters with vaginal adenocarcinoma**
- **Boys: reproductive organ abnormalitise**
- **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

❖ **In the male reproductive system they can alter:**

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

Eg:

- Exposure to phtalates, PCBs and organochlorine pesticides affect quality of sperm

- Lead reduces male fertility

- Carbon disulfide and some pesticides (chlordecone, ethylene dibromide and 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 in chips, packaged soups, meat seasonings)***
- ✓ **Obesity**
- ✓ **Anaesthesia** ***(enflurane)***
- ✓ **Soya products** ***(affects ability of sperm to enter the egg)***
- ✓ **Cocaine**
- ✓ **Chlorine-based chemicals (suspected)**
- ✓ **High scrotal temperature (laptop users)**

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

Eg: POPs (Persistent Organic Pollutants)

Stockholm Convention

- **CB-153 and DDE in semen of 149 Swedish fishermen from the eastern Baltic coast had 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

Human Reproduction – 28 April 2005

www.eshre.com

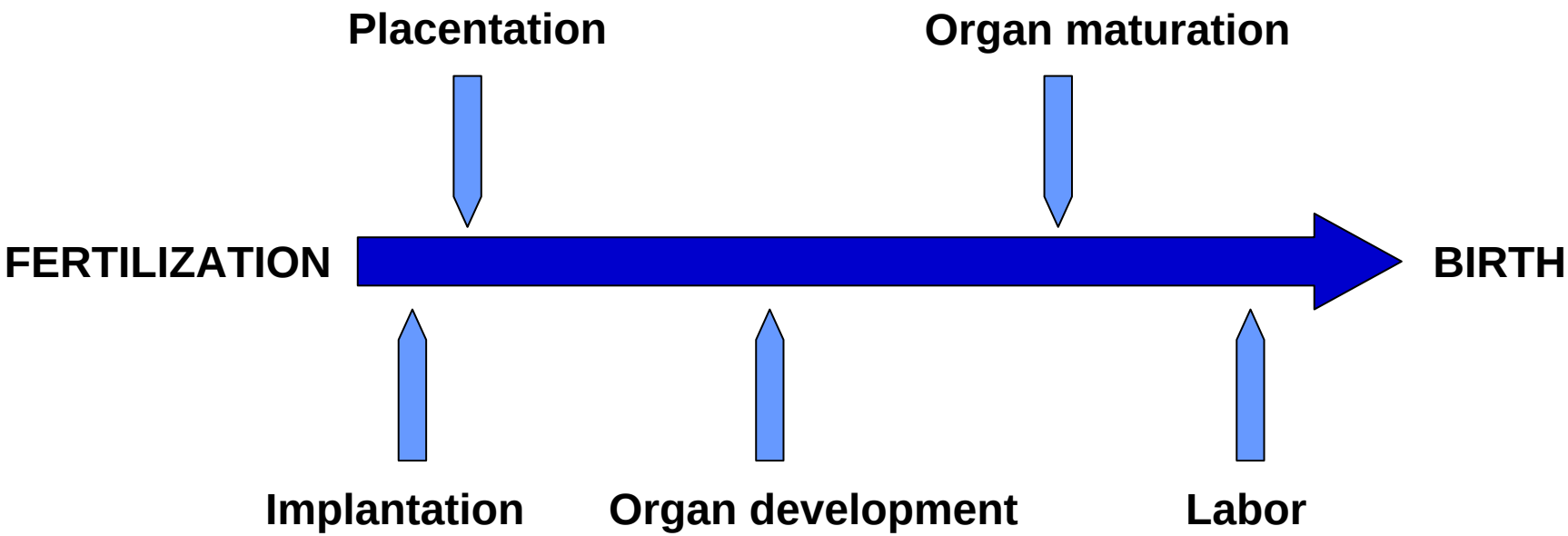
REPRODUCTIVE HEALTH

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:



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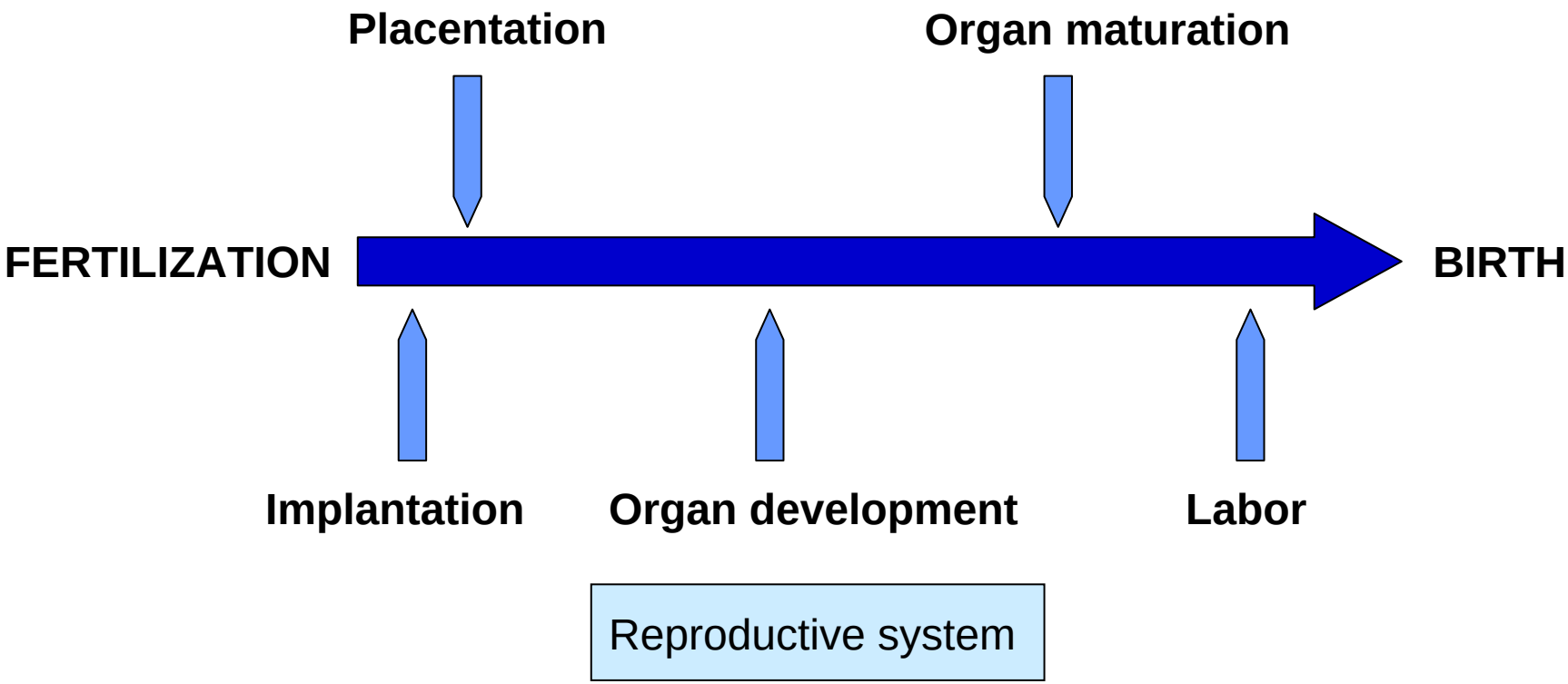

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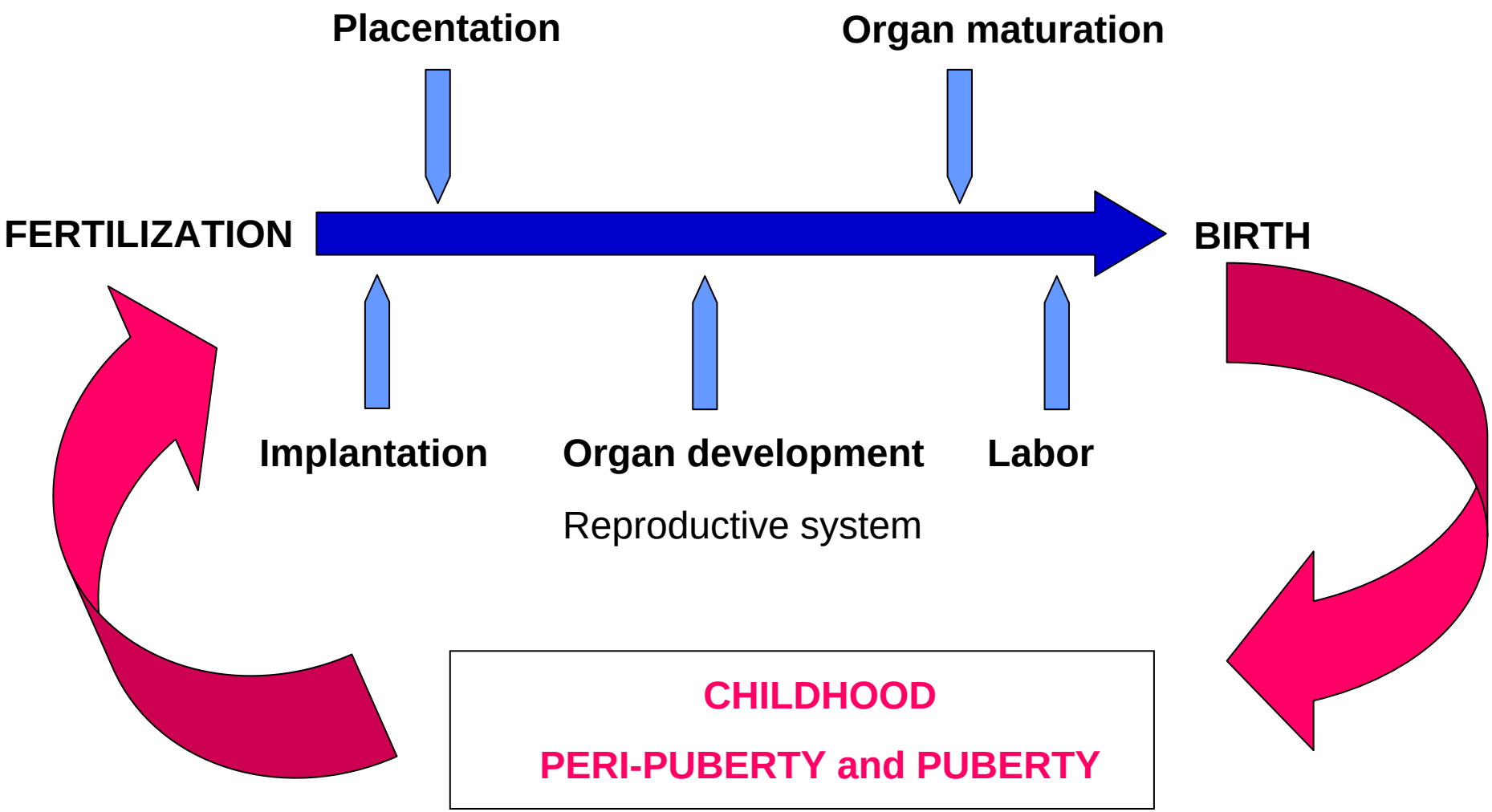


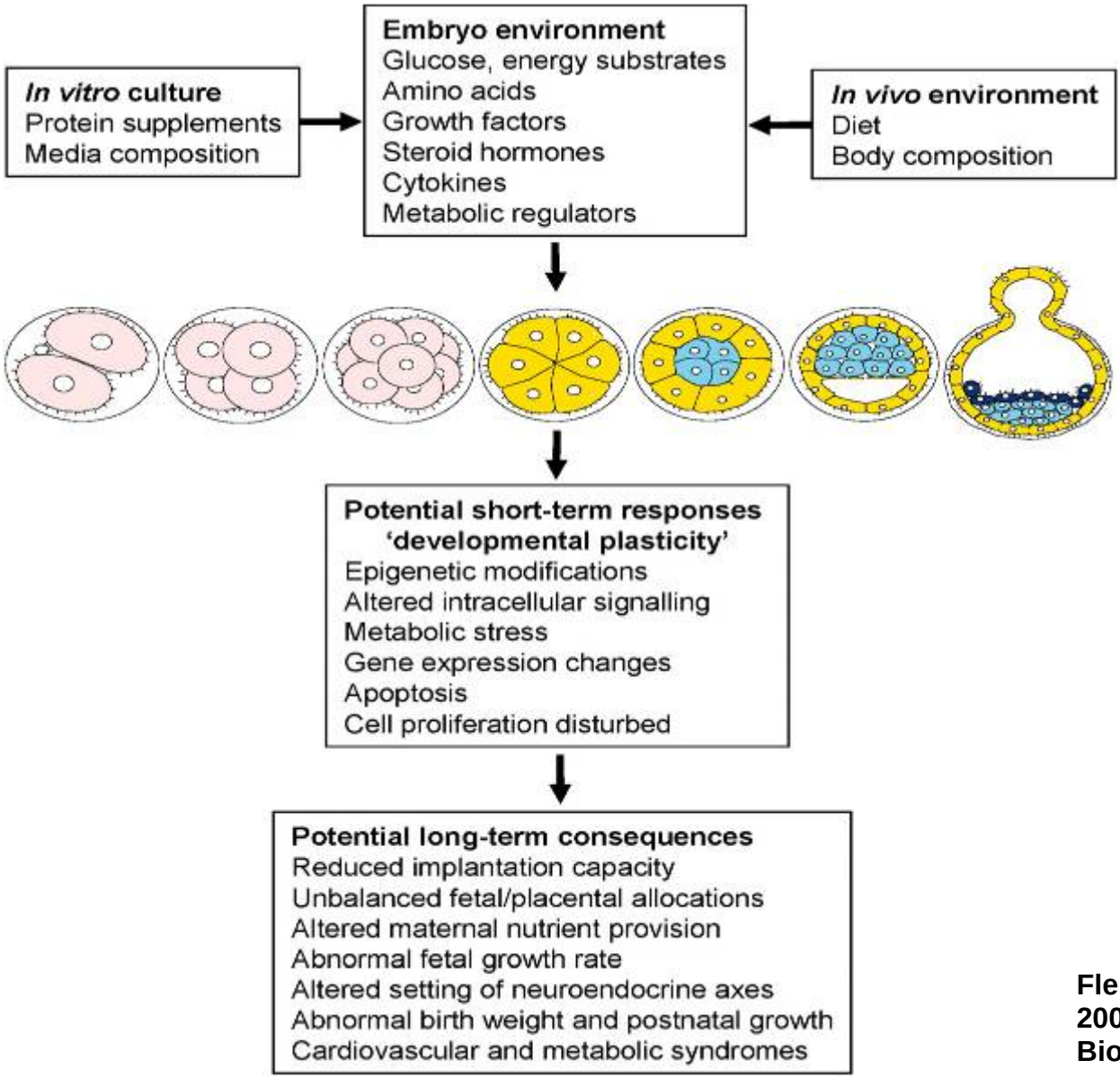
CRITICAL WINDOWS OF EXPOSURE IN REPRODUCTIVE HEALTH

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

CRITICAL WINDOWS OF EXPOSURE IN REPRODUCTIVE HEALTH

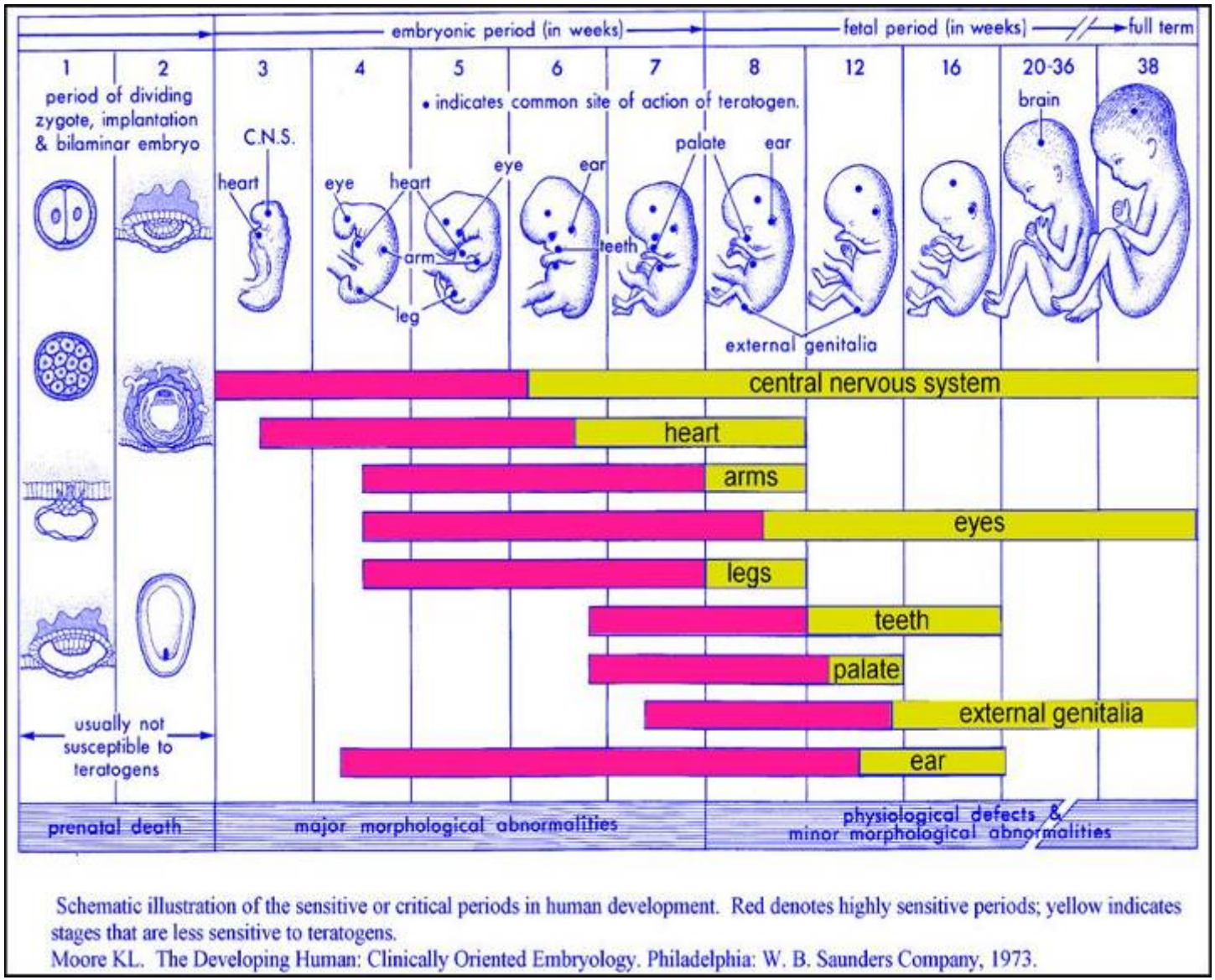
- **Pre-conceptional**
  - Damage to spermatozoal DNA may result in embryo death or fetal malformations
  - Numerical errors or structural changes in sex chromosomes – abnormal gonadal development and infertility (e.g. deletion in the Y chromosome)

Schematic representing the potential interactions between the environment of the embryo, in vitro/ in vivo, the embryo's short-term responses & long-term consequences...



Fleming, T. P. et al. Biol Reprod 2004;71:1046-1054
Biology of Reproduction

WINDOWS OF DEVELOPMENT



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

Moore, Elsevier Inc, 1973

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? Cryptorquidia? 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 O2 from uterus to placenta, raises maternal and fetal COHb levels

- PM 10 or PM2.5 linked to LBW or IUGR
- CO
- SO2
- 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)
- 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
- Eat seafood low in PCB and mercury contamination (salmon, canned tuna)

IF PREGNANT ALSO

- Try to find someone else to use household cleaners and pump gas for you.
- Paint baby room long before you conceive
- Don't use nail polish
- Eat canned salmon instead of canned tuna.
- Don't let people in your household smoke
- Calcium supplements minimize mineral loss from bone during pregnancy, therefore minimizing lead release form 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 prevents severe 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 dealing with reproductive health to be established in your workplace
- Do not rely only on material safety data sheets and be careful of misleading risk research.
- Determine if potential teratogenic agents can be replaced with safer materials.
- Be cautious … but not overly cautious.

Environment and reproductive health

WHO

"Improving children and mothers' 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/