3rd Euro-Asian Conference on Hazardous Waste and Human Health
Workshop on Children's Health and the Environment
Istanbul, Turkey. 27 March 2008

FETAL/ENVIRONMENTAL ORIGINS OF ADULT DISEASE

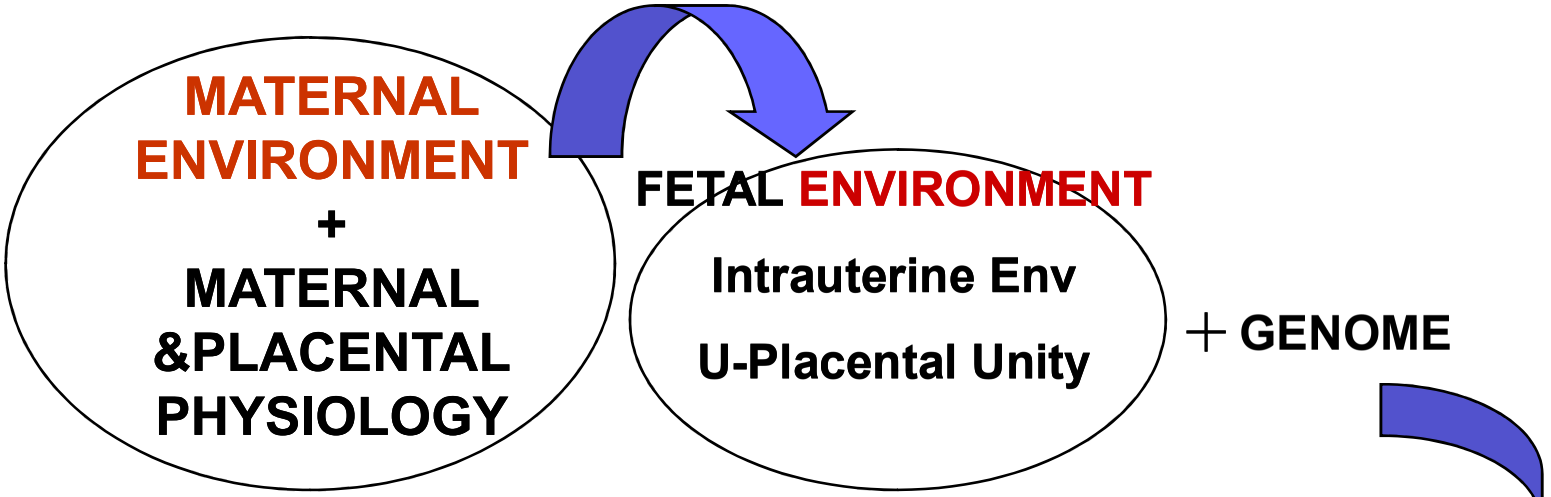
Children's Health and the Environment

WHO Training Package for the Health Sector

World Health Organization

www.who.int/ceh

Fetal Origins of Adult Disease



RESPONSES TO ADVERSE ENVIRONMENTS:

1. Accelerated maturation (↑ G-corticoid level)
2. Keeps nutrients (↓ growth & nutrition)
3. Pregnancy termination (abortion, prematurity)

ALTERATIONS:

- FETAL GROWTH
- INTERACTION PRE-AND POST-NATAL ENVIRONMENTS

FETAL ORIGIN OF DISEASE ⇨ **IMPACT ON PUBLIC HEALTH**

GENETIC MODIFICATIONS

Epigenetics:

Heritable changes in gene function that cannot be explained by changes in chromosomic system

3 Main types of epigenetic information:

- DNA methylation
- genomic imprinting
- Histone modification

- **Changes can be permanent or transient**
- **Some of them are part of normal development**
- **Some are affected by environment → altered gene expression (suppression/activation of genes)**

THRIFTY PHENOTYPE HYPOTHESIS

How does the fetus respond to an adverse environment?

By making irreversible changes in its development

- **Abnormal insulin secretion/action**
- **Reduced vascularity**
- **Reduced number of nephrons**

PREDICTIVE ADAPTIVE RESPONSES (PARs)

- The developing organism predicts its future environment
- Embryo/fetus depend on the information transmitted by the mother/placenta to evaluate/predict the present and future environments.
- **PARs**: decisions to change the course of development for future advantages
  - **Appropriate PARs**
  - **Inappropriate PARs**

Fetal Origins of Adult Disease

- Key concept: match/mismatch PARs

  Relationship between real and predicted postnatal environments determines disease risk

  - ✓ **Match: low risk of disease**
  - ✓ **No match: higher risk of disease**

- Nutritional signals:

  low food availability ⇒ insulin resistance

Fetal Origins of Adult Disease

- Very adverse environment → Death
- Less adverse environment → Alterations of
  - Maturity
  - Size
  - Growth

Other factors:
- Infections
- Genetics

Small newborn

(Prematurity)

Long-term consequences

Compensatory growth

WHO

IMPLICATIONS OF THESE MODELS

- "Lifestyle" disease
- Improve maternal and child health
- More research needed in:
  - Genetic changes
  - Windows of opportunity during plasticity periods?
  - Peri-conception period
  - Father and mother's exposure
  - Women's nutrition
  - Metabolic, cardiovascular, skeletal & other systems

BUT THE TIME FOR ACTION IS NOW

WHO

WHO

EXAMPLE OF AN INORGANIC CHEMICAL ARSENIC (AS)

- From natural erosion, pesticide run-off, coal burning, smelting, glass and electronic production waste
- Skin lesions and cancer, vascular and neurological disease, increased risk of cancer
- WHO guideline: 0.01 mg/L (ppm)
- Arsenic crosses the placenta
- Previous studies: *In utero* exposure to Arsenic linked to increased risk for stillbirth, and spontaneous abortion

EXAMPLE: ARSENIC AND THE ANTOFAGASTA STUDY

- **High Arsenic exposure in Antofagasta (Chile) from 1958 to 1970**

- **Study of exposed children (1958 – 1971): Increase in mortality from lung cancer and bronchiectasis when *in utero* + childhood exposure to arsenic in drinking water**

- Exposure in:	
Early childhood	*In utero* and early childhood
- Mortality due to:	
cancer SMR=7	SMR=6.1
bronchiectasia SMR=12	SMR=46.2

WHAT IS AN ENDOCRINE DISRUPTING CHEMICAL? (EDCS)

Exogenous substance or mixture that alters the function(s) of the hormonal system and consequently causes adverse effects in an intact *organism*, or its *progeny* or its *sub-population*

Natural

- **Phytoestrogens**
- **Fungal estrogens**

Synthetic

- **Hormones**
- **Some pesticides**
- **Industrial by-products ("dioxin-like")**
- **Pharmaceuticals**
- **Some persistent organic pollutants (POPs)**

EXAMPLES OF EFFECTS ON WILDLIFE

REPTILES: decline in alligator population by 90% after difocol, DDT, DDE chemical spill

- Smaller penis size
- Abnormal gonad morphology
- Altered sex steroid concentrations

FISH: reproductive alterations when exposed to sewage treatment waste

Fetal Origins of Adult Disease

Another type of cancer: Diethylstilbestrol as a model for environmental estrogens

- DES administered to pregnant women 1940-1960 for high-risk pregnancies but later to promote "healthier babies" as well.
- Female offspring developed clear-cell carcinoma of the vagina, vaginal adenosis, cervical ectropion, and other abnormalities.
- Males: reproductive tract abnormalities.

Has human cancer incidence resulting from DES exposure peaked? DES daughters are reaching post-menopause, the age of endometrial carcinoma…

- DES may be a model compound for other environmental agents with estrogenic potential.

PLASTICS

- Phthalates: solvents, soft plastics, and cosmetics
- Most US population exposed to phtalates
- Special population highly exposed
- Animals: reproductive and developmental toxicities
- Human studies: possible associations with
  - Altered semen quality
  - Shortened gestation
  - Reduced anogenital distance in baby boys
  - Premature breast development
  - Obesity

Hauser, Occupational and Environmental Medicine 2005

REPORT DETAILS ENVIRONMENTAL HARM TO FETUSES

- **Study by the Environmental Working Group and Commonweal on 10 babies born in 2004 (USA)**

- **Findings:**
  - 287 chemicals found.
  - 200 industrial chemicals and pollutants found in umbilical cord blood, as an average.
  - Among them: pesticides, consumer product ingredients and wastes from burning coal, gasoline and garbage.
  - 180 of these cause cancer in humans or animals,
  - 217 are toxic to the brain and nervous systems
  - 208 cause birth defects or abnormal development in animal tests.

Houlihan, Body Burden, The pollution in newborns, EWG, 2005

IF PREGNANT

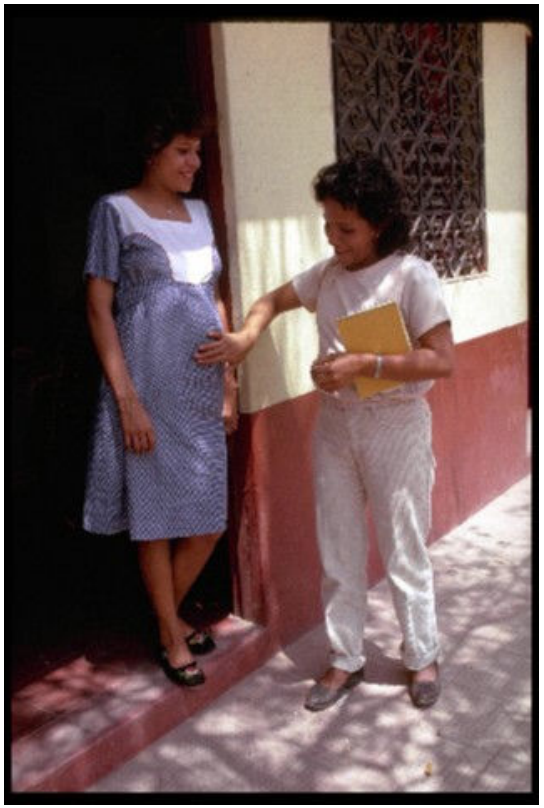
Many pregnancy/birth problems could be avoided through:

- **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.

HOW TO REDUCE EXPOSURE?



WHO

- Don't smoke! Nor stay near smokers
- Don't drink alcohol
- Eat food without additives
- …organic (without pesticides and preservers)
- Eat less meat and fat products
- Avoid fish rich in POPs and Hg (salmon, tuna,…)
- Avoid microwaving plastics
- Filter water at home
- Use few cosmetics and fragrances
- Don't use solvents
- Reduce the number of chemical cleaners at home

Table 2. Environmental exposure, susceptibility and preventive interventions, by developmental stages from preconception to adolescence

Developmental stage	Age-dependent biological and behavioural features	Environmental exposure	Adverse effects	Preventive interventions
Preconception	Young people and adults of reproductive age: lack of awareness of gonadal exposure	All environmental exposures	Potential for genotoxicity	Regulation and control of possible exposures for adults of reproductive age (workplace, waste sites) Information for adolescents and young people, employers and the general public
Embryo and fetus	Pregnant woman: mobilization of toxins from internal stores, transplacental passage, and subsequent exposure of the fetus Embryo and fetus: rapid cell growth and organ differentiation	All environmental exposures Ad hoc diagnostic investigations	Potential for teratogenicity	Regulations on occupational and other environmental exposures (such as ETS) and exposure during pregnancy Health information for couples
First two years	Organ development Immature metabolism Hand-to-mouth exploration Crawling and beginning to walk Eating the same foods every day	Pollutants in: food (such as breast-milk, formula milk and infant foods); air (particularly indoor); tap/well water; and mattresses, carpets, floors and soil Injuries and poisonings	Potential for organ damage, particularly to brain (synaptogenesis) and lungs (developing alveoli) Allergic sensitization	Regulation and control of water and sanitation, indoor and outdoor air pollutants, lead, pesticides and other chemicals in water and in infant foods Advice on preventing injuries
Preschool and school-age child	Growing independence Playground activities Critical vulnerability (in, for example, orphans, conflict and post-conflict situations, street children, and neglected children)	Injuries and poisonings Pollutants in: food (such as milk, fruit and vegetables), indoor and outdoor air and water Ultraviolet radiation and noise Violence and abuse	Potential for damage to brain and lungs (volume expansion), and carcinogenesis Injuries	Regulations, control of and information on outdoor and indoor pollutants, water and sanitation, food, ultraviolet radiation, noise and child labour Information for parents, teachers and children Prevention of abandonment and provision of social protection
Adolescence	Puberty Growth spurt Risk-taking behaviour Youth employment	Injuries and poisonings Pollutants in: food, outdoor and indoor air and water Ultraviolet radiation and electromagnetic fields Occupational exposure Violence and exploitation	Potential for damage to pubertal development, to all organs and systems and for carcinogenesis	Regulations on child labour, noise in discotheques, injury prevention, ETS Health information for young people Information and social protection

WHO: Training for the Health Sector

Improving the capacity to diagnose, prevent and manage paediatric diseases linked to the environment

New training materials:

- **Reproductive health and the Environment**

- **Environmental Health Criteria 237:**
  Principles for Evaluating Health Risks in children Associated with Exposure to Chemicals

http://www.who.int/ipcs/publications/ehc/ehc237.pdf

HECANET NEWSLETTER

- **HECANET is an international mailing list dedicated to promoting healthy environments for children.**
  - The list provides updates on:
  - the activities in the area,
  - advocacy tools and information resources,
  - relevant meeting announcements,
  - and reports on technical research and monitoring related to environmental risks to children's health

- **www.who.int/heca/infomaterials/hecanet/en/index.html**
- **To subscribe, send an email to: heca@who.int**