FETAL ORIGINS
OF ADULT DISEASE
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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

MATERNAL ENVIRONMENT
+ MATERNAL & PLACENTAL PHYSIOLOGY

FETAL ENVIRONMENT
Intrauterine Env
U-Placental Unit

+ GENOME
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**RESPONSES TO ADVERSE ENVIRONMENTS:**

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

**ALTERATIONS:**

- Fetal growth
- Interaction pre-and post-natal environments

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How does the fetus respond to an adverse environment – e.g.: nutritional?
By making irreversible changes in its development

- Abnormal insulin secretion/action → Type II diabetes
- Reduced vascularity → Hypertension
- Reduced nephron number → CV disease
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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
Developmental plasticity:

- **Plasticity** # **Disruption**

- **Developmental plasticity**: normal processes that allow a range of phenotypes to develop from a single genotype

- **Disruption**: alteration of the developmental program

- Sometimes, the difference is not evident
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DYNAMIC DEVELOPMENTAL PHYSIOLOGY
WINDOWS OF DEVELOPMENT

Moore, Elsevier Inc, 1973

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.

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- 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
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Very adverse environment → Death
Less adverse environment → Alterations of
- Maturity
- Size
- Growth
Small newborn
(Prematurity)

Other factors:
- Infections
- Genetics

Long-term consequences
Compensatory growth
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FETAL AND INFANT PROGRAMMING

- Peri-conception period
  - Crucial nutrients: vitamin B12, folate, choline, methionine, glicine

- Birth: environmental transition in human development

- Neonate is in a phase of plasticity

- The neonate perceives as his/her environment what the health care provider/mother presents
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**Suspected** fetal/environmental origins of disease:

- Herbicides → Parkinson disease
- Insecticides
- Manganese
- Pb, Hg, PCBs → Dementia
- Different chemicals → Cancer
- Undernutrition → Osteoporosis
- Poor early growth → Ageing
- Undernutrition → COPD
- Anxiety disorders → Stress
- ? → Alzheimer disease
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IMPLICATIONS OF THESE MODELS

- "Lifestyle" disease

- Improve maternal and child health and their environments

- More research needed in:
  - Genetic changes
  - Peri-conception period
  - Women's nutrition
  - Metabolic, cardiovascular, skeletal & other systems
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