TRAINING FOR THE HEALTH SECTOR

Training Course in Reproductive Health / Sexual Health Research

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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

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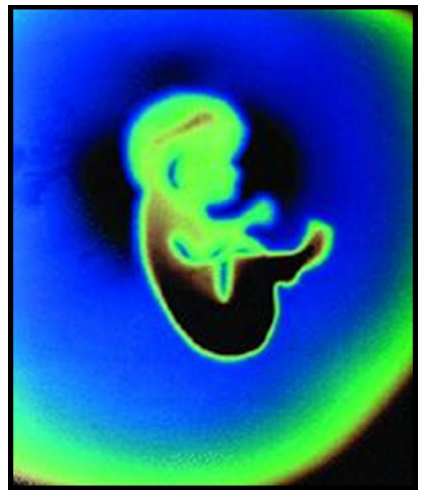
Fetal Origins of Adult Disease

MATERNAL ENVIRONMENT
+
MATERNAL & PLACENTAL PHYSIOLOGY

FETAL ENVIRONMENT
Intrauterine Env
U-Placental Unit

+ GENOME



Fetal Origins of Adult Disease

MATERNAL ENVIRONMENT + MATERNAL & PLACENTAL PHYSIOLOGY

FETAL ENVIRONMENT

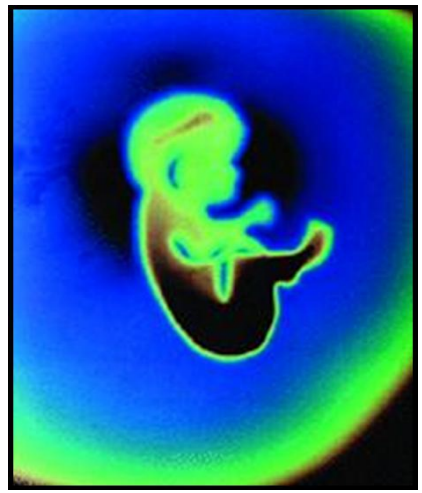
Intrauterine Env

U-Placental Unity

+ GENOME

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

Fetal Origins of Adult Disease

EHP

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**

PREDICTIVE ADAPTIVE RESPONSES (PARs)

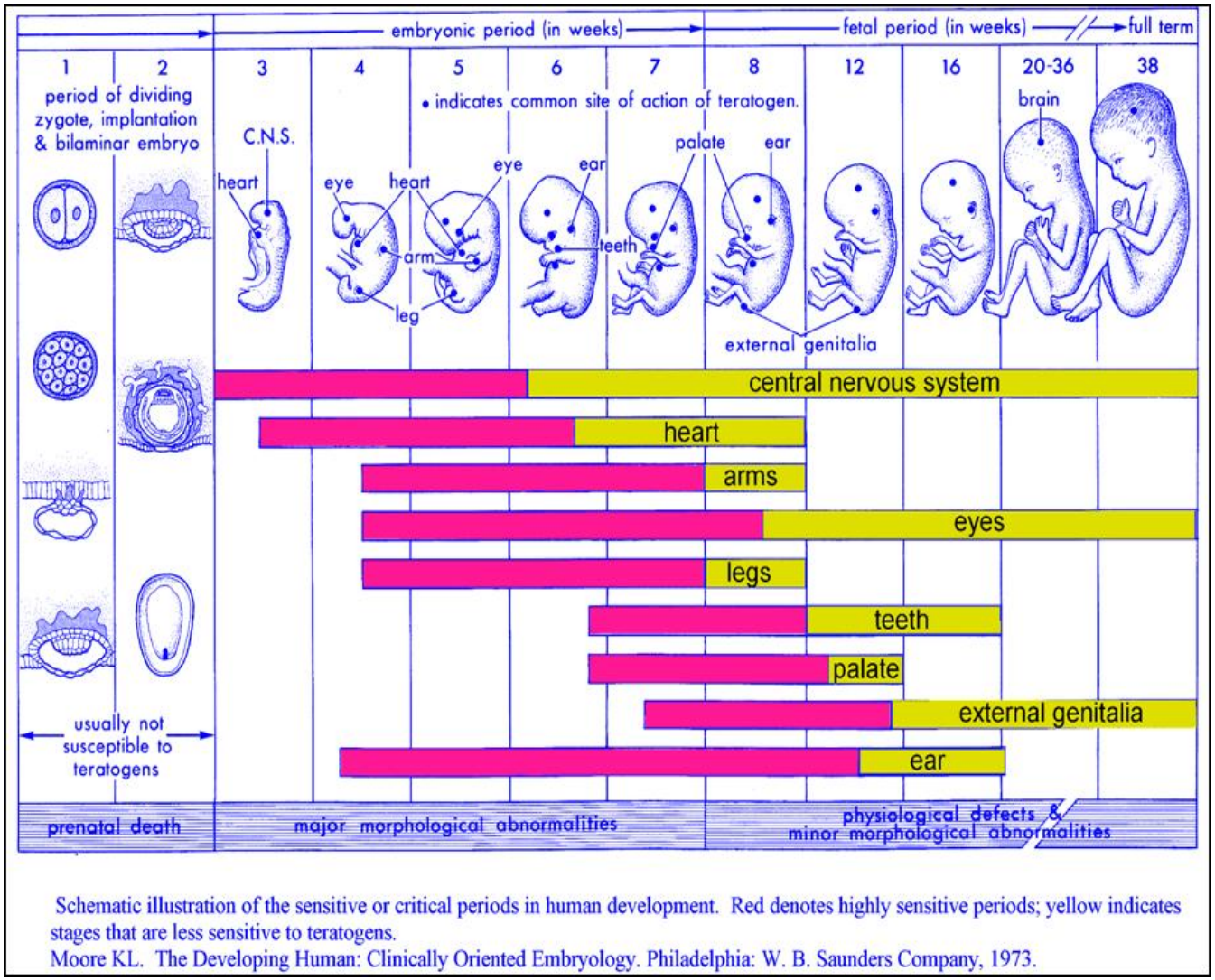
- The developing organism predicts its future environment
- Embryo/fetus depend on the information transmitted by the mother/placenta to evaluate/predict the present and future environments.
- **PARs**: decisions to change the course of development for future advantages
  - **Appropriate PARs**
  - **Inappropriate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

DYNAMIC DEVELOPMENTAL PHYSIOLOGY

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

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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

Other factors:
- Infections
- Genetics

Small newborn

(Prematurity)

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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<u>Suspected</u> 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**

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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