Early Life Exposure and Disease Health Risk

Shuk-Mei Ho, PhD

Jacob G. Schmidlapp Professor & Chair
Department of Environmental Health, University of Cincinnati
Director, Center for Environmental Genetics,
Director, Cincinnati Cancer Center,
Cincinnati Veteran Affairs Medical Center
Cincinnati, Ohio

Co-authors: Ana Cheong, Sarah To, Vinothini Janakiram,
Pheruza Tarapore, Yuet-Kin Leung
Factors that contribute to increased cancer risk

Effect of early life exposures to environmental agents on health diseases:
- prostate cancer
- uterine cancer
- metabolic diseases
- reproduction
Twin studies show that there must be factors separate from DNA that impact health and longevity.

Environmental differences can make one twin more vulnerable to disease than the other (e.g., smoking and diet).

Genomic DNA is virtually identical.

Their health outcome and behavior may change over time depending on the environment after birth.
Cancer incidence is higher in immigrants: Incident rate increases in subsequent generations

Effects of lifestyle, dietary, environmental factors?

Popkin and Udry, 1998; Singh and Hiatt, 2006; Ziegler et al, 1993
Bisphenol A (BPA) - the endocrine disruptor

Production of 1.6 billion pounds in North America

95% of adults surveyed have detectable concentrations of total urinary BPA (Calafat et al 2005)

BPA is ubiquitously present in the environment
Epigenetics serves as an interface between the environment and the inherited genome.
Early origins of human diseases

Epidemiologic studies now support an early origin of adult human diseases.

Example:
association between low birth weight and a greater risk of coronary heart disease, hypertension, stroke, depression, type 2 diabetes, and osteoporosis in later life
Developmental Plasticity: Windows of Susceptibility

Prenatal  Neonatal  Prepubertal  Pubertal  Sexual Maturity (Pregnancy)

fetus  newborn  child  adolescent  adult  elderly adult

Is breast cancer of fetal origin?
Hypothesis

*In utero* exposure to dietary fats and environmental agents increases breast cancer risk later in life.

**Diet**

Fat in Cultural Diets

**Environment**

Bisphenol A

- Altered epigenome, gene expression, and steroid hormonal levels
- Changes in cell behavior and morphology
- Increased breast cancer risk
*In utero* exposure to estradiol and bisphenol A reprograms prostate cancer (PCa) risk.

**Before birth**
- **Caucasians**
  - Lower estradiol level
- **African-Americans**
  - Higher estradiol level

**Young**
- Lower PCa incidence

**Old**
- Higher PCa incidence

**Bisphenol A**

Henderson and Ross 1988
Neonatal estrogen reprogramming increases later life prostate cancer risk

Sprague Dawley rat
No estrogen (E)

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  → Adult hormonal Treatment on PND 90-200 → Low cancer Incidence (30%)
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Neonatal estrogen treatment on post-natal day (PND)1, 3, 5

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E → Adult hormonal Treatment on PND 90-200 → E
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High cancer Incidence ≈ (100%)

Noble rat

Ho, Tang and Prins, Cancer Res 2006
In utero exposure to diethylstilbestrol induces uterine cancer risk and infertility in later life.

Diethylstilbestrol (DES) - Synthetic estrogen

Increased incidence of ectopic pregnancy

Reproductive Tract Abnormalities
- normal cervix with a “hood”
- normal a “T” shaped uterus

Increased risk of uterine adenocarcinoma

Higher miscarriage and infertility rates

Ho, Tang and Prins, Cancer Res 2008
Paternal exposure to high fat diet and environmental agents increases health risk in offspring.

Fullston et al, Physiol rep, 2015; Carone et al, Cell, 2010
Early life exposures to environmental agents and different lifestyle factors affects later-life cancer risk

The End
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