Preconception Health & Health Care: A Life-Course Perspective

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August 3, 2010
Why Preconception Care?
Why Preconception Care?

- Early prenatal care is too late.
Early Prenatal Care Is Too Late To Prevent Some Birth Defects

- The heart begins to beat at 22 days after conception
- The neural tube closes by 28 days after conception
- The palate fuses at 56 days after conception
- Critical period of teratogenesis – **Day 17 to Day 56**
Early Prenatal Care Is Too Late To Prevent Implantation Errors

Early Prenatal Care Is Too Late from A Life-Course Perspective

☐ A way of looking at life not as disconnected stages, but as an integrated continuum
Early Programming
Barker Hypothesis
Birth Weight and Hypertension

Maternal Stress & Fetal Programming
Prenatal Stress & Programming of the Brain

- **Prenatal stress (animal model)**
  - **Hippocampus**
    - Site of learning & memory formation
    - Stress down-regulates glucocorticoid receptors
    - Loss of negative feedback; overactive HPA axis
  - **Amygdala**
    - Site of anxiety and fear
    - Stress up-regulates glucocorticoid receptors
    - Accentuated positive feedback; overactive HPA axis

Prenatal Programming of the Hypothalamic-Pituitary-Adrenal Axis

**Epigenetics**

**Volume Controls for Genes**

The DNA sequence is not the only code stored in the chromosomes. So-called epigenetic phenomena of several kinds can act like volume knobs to amplify or mute the effect of genes. Epigenetic information is encoded as chemical attachments to the DNA or to the histone proteins that control its shape within the chromosomes. Among their many functions, the epigenetic volume controls muffle parasitic genetic elements, called transposons, that riddle the genome.

1. Chemical changes to a chromosome can force some parts of it to condense into a tight, inaccessible mass or can recruit repressor proteins. In both cases, the genes on that part of the DNA temporarily stop working.

2. Chromosomes are made of chromatin, a melange of DNA, proteins and other chemicals. Inside a chromosome, the double helix loops around spools of eight histone proteins to form a rosary-like chain of nucleosomes.

3. An intricate histone code—written in chemical tags stuck to the histones' tails (above)—governs gene expression as well. Acetyl tags usually amplify nearby genes, whereas acetyl-removing enzymes mute them. But the rest of the code remains to be deciphered.

4. Genes can also be suppressed by methyl tags that stick directly to the DNA, usually at places where a C base is followed by a G. Whether DNA methylation turns down genes independently or only in combination with histone tags is still a mystery.

5. Transposons, also called jumping genes, can clone themselves and then insinuate the copies into distant sections of the genome, sometimes disabling or hyperactivating genes. One major function of DNA methylation seems to be the suppression of transposons, which make up almost half the human genome.

_Gibbs WW. The Unseen Genome: Beyond DNA. Scientific American 2005_
Epigenetics
Same Genome, Different Epigenome

Prenatal Programming of Childhood Obesity
Epidemic of Childhood Overweight & Obesity

Children 6-18 Overweight

Source: National Center for Health Statistics, National Health and Nutrition Examination Survey

Note: Estimate not available for 1976-1980 for Hispanic; overweight defined as BMI at or above the 95th percentile of the CDC BMI-for-age growth charts
Prenatal Programming of Childhood Overweight and Obesity

Jennifer S. Hwang - Tiffany A. Lou - Michael C. Lu

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Abstract. Objective: To review the scientific evidence for prenatal programming of childhood overweight and obesity, and discuss its implications for MCH research, practice, and policy.

Methods: A systematic review of observational studies examining the relationship between prenatal exposures and childhood overweight and obesity was conducted using MOOSE guidelines. The review included literature posted on PubMed and MRC Summit and published between January 1975 and December 2005. Prenatal exposures to maternal diabetes, smoking, and alcohol were examined, and primary study outcome was childhood overweight or obesity as measured by body mass index (BMI) for children ages 5 to 21.

Results: Four included studies of prenatal exposure to maternal diabetes found higher prevalence of childhood overweight or obesity among offspring of diabetic mothers, with the highest quality study reporting an odds ratio of adolescent overweight of 1.4 (95% CI 1.0–1.9). The Dutch famine study found that exposure to maternal malnutrition in early, but not later, gestation was associated with increased odds of childhood obesity (OR 1.9, 95% CI 1.5–2.4). All eight included studies of prenatal exposure to maternal smoking showed significantly increased odds of childhood overweight and obesity, with most odds ratios clustering around 1.5 to 2.0. The biological mechanisms mediating these relationships are unknown but may be partially related to programming of insulin, leptin, and glucocorticoid resistance in early pregnancy.

Conclusions: Our review supports prenatal programming of childhood overweight and obesity. MCH research, practice, and policy need to consider the prenatal period a window of opportunity for obesity prevention.

Keywords: Prenatal programming - Childhood obesity - Overweight - Developmental programming - Fetal programming - Maternal malnutrition - Cigarette smoking

Childhood overweight and obesity is a growing problem in the United States and worldwide. The prevalence of childhood overweight in the U.S. tripled between 1980 and 2000 [1]. Today, approximately 1 in 6 (16%) U.S. children are overweight with significant racial-ethnic disparities. For example, nearly 1 in 4 (23%) non-Hispanic Black girls ages 6 to 11 are overweight, a prevalence twice that of non-Hispanic white girls (11%).

Overweight and obesity has significant lifelong consequences on the health and wellbeing of children [2, 3]. Childhood obesity is associated with early-onset Type II diabetes mellitus, hypertension, metabolic syndrome, and sleep apnea. It is also associated with cognitive or intellectual impairment and social exclusion and stigmatization as parts of a vicious cycle including school avoidance [3]. Childhood obesity tracks strongly into adulthood [4, 5]; obesity beyond
Prenatal Programming of Childhood Obesity

Maternal Diabetes & Intrauterine Hyperglycemia

Intrauterine Hyperinsulinemia (Fetal Pancreatic β Cells)

Preadipocyte Differentiation

Programmed Insulin Resistance

Prenatal & Postnatal Hyperleptinemia

Adipocyte Hyperplasia

Postnatal Hyperinsulinemia

Prenatal & Postnatal Hyperleptinemia

Hypothalamic Leptin Resistance

Pancreatic β-Cell Leptin Resistance

Hyperphagia

Hyperinsulinism

Adipogenesis
Cumulative Pathways
Allostasis: Maintain Stability through Change

Allostastic Load: Wear and Tear from Chronic Stress

<table>
<thead>
<tr>
<th>Stressed</th>
<th>Stressed Out</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased cardiac output</td>
<td>Hypertension &amp; cardiovascular diseases</td>
</tr>
<tr>
<td>Increased available glucose</td>
<td>Glucose intolerance &amp; insulin resistance</td>
</tr>
<tr>
<td>Enhanced immune functions</td>
<td>Infection &amp; inflammation</td>
</tr>
<tr>
<td>Growth of neurons in hippocampus &amp; prefrontal cortex</td>
<td>Atrophy &amp; death of neurons in hippocampus &amp; prefrontal cortex</td>
</tr>
</tbody>
</table>
Sequelae of Preterm Birth

- 75% Perinatal Perinatal Mortality
- 50% Neurologic Disabilities
- 12% Term Births

- Preterm Birth
Racial & Ethnic Disparities
Preterm Births < 37 Weeks

Percent of Live Births

African American: 17.9%
White: 11.5%
Year 2010 Goal: 14%

NCHS 2006
Racial & Ethnic Disparities
Very Preterm Births < 32 Weeks

Percent of Live Singleton Births

African American: 4.05
White: 1.63
Year 2010 Goal: 1.63
NCHS 2006
Racial & Ethnic Disparities
Infant Mortality

Deaths Per 1,000 Live Births

African American: 13.7
White: 5.7

Year 2010 Goal

NCHS 2006
Vulnerability to preterm delivery may be traced to not only exposure to stress & infection during pregnancy, but host response to stress & infection (e.g. stress reactivity & inflammatory dysregulation) patterned over the life course (early programming & cumulative allostatic load).
An important objective of preconception care is to restore allostasis to women’s health before pregnancy.
Kaplan-Meier plots of cumulative probability of survival without admission or death from ischemic heart disease after first pregnancy in relation to preterm birth
Why Preconception Care?

Summary

☐ Early Prenatal Care Is Too Late
  ■ To prevent some birth defects
  ■ To prevent implantation errors
  ■ To restore allostasis quickly enough to optimize fetal programming
Why Preconception Care?
Before, Between, and Beyond Pregnancy
Put the W Back in MCH
INTERCONCEPTION CARE