Improving Preconception Health & Healthcare in Louisiana

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“If you want 1 year of prosperity, grow grain. If you want 10 years of prosperity, grow trees. If you want 100 years of prosperity, grow people.”

Chinese Proverb
“If you want to grow healthier people, you start by improving women’s health before pregnancy.”

Not A Chinese Proverb
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
Early Prenatal Care Is Too Late
To Prevent Implantation Errors

Life-Course Perspective

- A way of looking at life not as disconnected stages, but as an integrated continuum
Life Course Perspective

Life Course Perspective

- Early programming
- Cumulative pathways
Early Programming
Barker Hypothesis

Birth Weight and Hypertension

Barker Hypothesis
Birth Weight and Insulin Resistance Syndrome

Odds ratio adjusted for BMI

Birthweight (lbs)

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 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 mélange 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
The bar chart illustrates the percentage of children aged 6-18 who were overweight from 1976-1980, 1988-1994, and 1999-2002. The data shows a significant increase in overweight rates for all ethnic groups during these periods.

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. Huang - Tiffany A. Lou - Michael C. Lu

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. Method: A systematic review of observational studies examining the relationship between prenatal exposure and childhood overweight and obesity was conducted using MOOSE guidelines. The review included literature posted on PubMed and MEDLINE and published between January 1973 and December 2005. Prenatal exposures to maternal diabetes, malnutrition, and cigarette smoking were examined, and primary study outcome was childhood overweight or obesity as measured by body mass index (BMI) for children ages 5 to 19. Results: Forty-two 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 late, 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 mean 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 utero. Conclusion: Our review supports prenatal programming of childhood overweight and obesity. MCH research, practice, and policy need to consider the prenatal period as a window of opportunity for obesity prevention. Keywords: Prenatal programming - Childhood obesity - Overweight - Developmental programming - Fetal programming - Maternal diabetes - 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 19 are overweight, a prevalence almost twice that of non-Hispanic white girls [1].

Overweight and obesity has significant lifelong consequences on the health and well-being of children [2, 3]. Childhood obesity is associated with early-onset Type II diabetes mellitus, hypertension, metabolic syndrome, and sleep apnea, and is also associated with cognitive and 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
      - Adipocyte Hyperplasia
    - Programmed Insulin Resistance
      - Adipocyte Hyperplasia
    - Prenatal & Postnatal Hyperleptinemia
      - Postnatal Hyperinsulinemia
        - Hypothalamic Leptin Resistance
        - Hyperphagia
        - Hyperinsulinism
          - Adipogenesis
          - Pancreatic β-Cell Leptin Resistance
            - Hyperinsulinism
              - Adipogenesis
Cumulative Pathways
Allostasis: Maintain Stability through Change

Allostastic Load: Wear and Tear from Chronic Stress

## Stressed vs. Stressed Out

<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>
Allostasis & Allostatic Load

Rethinking Preterm Birth
Preterm Birth

- 12.3% Preterm Birth
- 36% Infant Mortality
- 50% Neurologic Disabilities

NCHS 2010
Racial & Ethnic Disparities
Preterm Births < 37 weeks

Percent of Live Births

Year 2010 Goal

NCHS 2010
Racial & Ethnic Disparities
Very Preterm Births < 32 Weeks

Percent of Live Singleton Births

<table>
<thead>
<tr>
<th>Race</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black</td>
<td>4.17</td>
</tr>
<tr>
<td>White</td>
<td>1.64</td>
</tr>
</tbody>
</table>

Year 2010 Goal

NHS 2010
Racial & Ethnic Disparities
Infant Mortality

Deaths Per 1,000 Live Births

Year 2010 Goal

Black: 13.2
White: 5.6

NCHS 2010
Rethinking Preterm Birth

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)
Kaplan-Meier plots of cumulative probability of survival without admission or death from ischemic heart disease after first pregnancy in relation to preterm birth
Preconception Health and Health Care: Why Is It Important?
Take Home Message #1

- Even early prenatal care may be too late
  - To prevent some birth defects
  - To prevent implantation errors
  - To restore allostasis quickly enough to optimize fetal programming
Take Home Message #2

- An important objective of preconception care is to restore allostasis and optimize women’s health before pregnancy.
Take Home Message #3

- If you want to grow healthier people in Louisiana, you start by improving women’s health before pregnancy.
Interconception Care
The definition of insanity is doing the same thing over and over and expecting different results

Benjamin Franklin
"We must become the change we want to see."

- MOHANDAS GANDHI
“Never, ever, think outside the box.”