Before, Between and Beyond Pregnancy: From Concept to Practice

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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
- Improving MCH: A life-course perspective
Early Programming
Barker Hypothesis
Birth Weight and Coronary Heart Disease

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

Fig. 1. Schematic representation of the hypothalamic-pituitary-adrenal (HPA) axis. GR, glucocorticoid receptor; MR, mineralocorticoid receptor; PVN, paraventricular nucleus; CRH, corticotropin-releasing hormone; AVP, arginine vasopressin; ACTH, adrenocorticotrophic hormone.

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 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 2003
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 & Obesity

Jennifer S. Huang, Tiffany A. Lee, 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.

Methods: A systematic review of observational studies examining the relationship between prenatal exposures and childhood overweight and obesity was conducted using MEDLINE citations and Pubmed searches. The review included literature published from 1975 to December 2005. Prenatal exposures to maternal diabetes, smoking, and maternal obesity 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: Most of the 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 1.1 (95% CI 1.0-1.2). The Dutch folic acid 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 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 ghrelin concentration and function.

Conclusions: 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 - Gestational 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 (25%) non-Hispanic black girls ages 6 to 11 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. It is also associated with cognitive and intellectual impairment and social exclusion and stigmatization as part of a vicious cycle including school avoidance (3). Childhood obesity tracks strongly into adulthood (4, 5).

Disclaimer: The opinions expressed in this paper are the author’s and do not necessarily reflect the views or policies of the institutions with which the author is affiliated.

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Prenatal Programming of Childhood Obesity

Maternal Diabetes & Intrauterine Hyperglycemia

Intrauterine Hyperinsulinemia (Fetal Pancreatic β Cells)

Preadipocyte Differentiation
- Adipocyte Hyperplasia

Programmed Insulin Resistance

Prenatal & Postnatal Hyperleptinemia

Prenatal Hyperinsulinemia

Postnatal Hyperinsulinemia

Hypothalamic Leptin Resistance
- Hyperphagia

Pancreatic β-Cell Leptin Resistance
- Hyperinsulinism
- Adipogenesis

Prenatal Programming of Childhood Obesity
Cumulative Pathways
Allostasis:
Maintain Stability through Change

Allostastic Load: Wear and Tear from Chronic Stress

HPA Axis & Immune System
Chikanza 2000
Stressed vs. Stressed Out

- **Stressed**
  - Increased cardiac output
  - Increased available glucose
  - Enhanced immune functions
  - Growth of neurons in hippocampus & prefrontal cortex

- **Stressed Out**
  - Hypertension & cardiovascular diseases
  - Glucose intolerance & insulin resistance
  - Infection & inflammation
  - Atrophy & death of neurons in hippocampus & prefrontal cortex
Allostasis & Allostatic Load

Rethinking Preterm Birth
Sequela of Preterm Birth

- Term Births: 75%
- Preterm Birth: 12%
- Perinatal Mortality: 50%
- Neurologic Disabilities: 75%
Racial & Ethnic Disparities
Infant Mortality

Deaths Per 1,000 Live Births

African American: 13.6
White: 5.7

Year 2010 Goal

NCHS 2007
Racial & Ethnic Disparities Preterm Births < 37 Weeks

<table>
<thead>
<tr>
<th>Race</th>
<th>Percent of Live Births</th>
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<tbody>
<tr>
<td>African American</td>
<td>18.4</td>
</tr>
<tr>
<td>White</td>
<td>11.7</td>
</tr>
</tbody>
</table>

Year 2010 Goal

NCHS 2007
Racial & Ethnic Disparities
Very Preterm Births < 32 Weeks

Percent of Live Singleton Births

African American: 4.17
White: 1.64

Year 2010 Goal

NCHS 2007
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).
Preterm Birth & Maternal Ischemic Heart Disease

Kaplan-Meier plots of cumulative probability of survival without admission or death from ischemic heart disease after first pregnancy in relation to preterm birth

Smith et al Lancet 2001;357:2002-06
Improving MCH: A Life-Course Perspective
Women’s Health:  
A Life-Course Perspective
Improving MCH: 
A Life-Course Perspective

The life-course perspective suggests a need for an expanded approach to improve perinatal health, one that emphasizes not only risk reduction during pregnancy, but also health promotion and optimization before and between pregnancies and, indeed, across the life course. The approach needs to be both clinical and population-based, addressing individual factors as well as social determinants of perinatal health.
Access
Improve Healthcare Access

*Before, Between, Beyond Pregnancy*

- **Preconception & interconception care**
  - Mandated coverage & provision to override exclusions based on preexisting conditions
  - Covered service under FEHBP
  - Medicaid waiver (e.g. Illinois Healthy Women Initiative)

- **Comprehensive women’s healthcare over the life course.**
Interconception Care
Quality
Enhance service integration

*Before, Between, Beyond Pregnancy*

- Medical home for pregnancy
  - California’s Comprehensive Perinatal Services Program (CPSP)

- Wellness homes across the life course
  - Hope Street Family Center in Los Angeles
  - DC Developing Families Center
MCH Life-Course Organization

Early Childhood
- Early Head Start
- Head Start
- UPK
- Choir Academy

Child Welfare
- Preventive Services
- Foster Care Services
- Parenting Workshop
- Newborn Home Visiting
- COPS Waiver

Legislative Agenda
- Reauthorize Healthy Start
- SCHIP
- Minimum Wage Legislation
- Women’s Health Financing

Economic Opportunities
- Harlem Works
- Financial Literacy
- LPN RN Training Program
- Union Employment
- Micro Lending Savings
- Empowerment Zone

Health System
- Case Management - Title V Funds
- Health Education - Regionalization
- Outreach - Harlem Hospital
- Perinatal Mood Disorders - Birthing Center
- Interconceptional Care

Housing
- Home Ownership
- Affordable Housing
- Base Building - St. Nicks
Wellness
Invest in Wellness

Before, Between, Beyond Pregnancy

☐ Wellness Trust
- Fund prevention (VAT, sin tax, etc)
- Set national priorities on prevention (USPSTF)
- Effective delivery systems
- Develop an information technology backbone
- Incentivize prevention

☐ Children’s Trust
Family & Community
Strengthen Families & Communities
*Before, Between, Beyond Pregnancy*

- Fatherhood initiatives
- Best start zones
Reproductive Social Capital

- Features of social organization (e.g. networks, norms, and social trust) that facilitate coordination and cooperation to promote reproductive health within a community.
Reproductive Social Capital

- 100 Intentional Acts of Kindness toward a Pregnant Woman
Education
Educational Development

1. Preconception and prenatal care
2. Parenting education
3. Child care
4. Universal Preschool
5. Early Head Start and Head Start
6. K-12 – small class size, teacher quality, standards
7. After school and summer programs
8. Youth development
9. Health education/physical education
10. Comprehensive school health clinics
Educational Development

- Early Childhood programs
- After-school programs
- Summer Programs
- Comprehensive school health clinics

$156 billion
Environment
“Now that you’re here,
the word of the Lorax seems perfectly clear.
**UNLESS** someone like you
Cares a whole awful lot,
Nothing is going to get better.
   It’s not.
   “SO...
Catch!” calls the Once-ler.
   He lets something fall.
   “It’s a Truffula Seed.
   It’s the last one of all!
You’re in charge of the last of the Truffula Seeds.
   And Truffula Trees are what everyone needs.
   Plant a new Truffula. Treat it with care.
   Give it clean water. And feed it fresh air.
   Grow a forest. Protect it from axes that hack.
Then the Lorax
   And all of his friends
   May come back.”

- Dr. Seuss, *the Lorax*
Policy
## Maternity Leave

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<tr>
<th>Country</th>
<th>Weeks before delivery</th>
<th>Weeks after delivery</th>
<th>Salary</th>
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<tbody>
<tr>
<td>USA</td>
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<td>6</td>
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</tr>
<tr>
<td>UK</td>
<td>10 + 5 days</td>
<td>25 + 5 days</td>
<td>Yes</td>
</tr>
<tr>
<td>France</td>
<td>6 + 3 days</td>
<td>8 + 5 days</td>
<td>Yes</td>
</tr>
<tr>
<td>Germany</td>
<td>7 + 3 days</td>
<td>8</td>
<td>Yes</td>
</tr>
<tr>
<td>Italy</td>
<td>8 + 5 days</td>
<td>12 + 6 days</td>
<td>Yes</td>
</tr>
<tr>
<td>Spain</td>
<td>16</td>
<td>6</td>
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</tr>
<tr>
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<td>4</td>
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<tr>
<td>Czech Republic</td>
<td>6</td>
<td>22</td>
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</table>
Expand Parental Leave

- Only 45% of parents working in private sector have guaranteed unpaid parental leave through FMLA
- Only 5% have paid parental leave

Expand paid leave
- Unemployment insurance
- Temporary disability insurance
- New social insurance
- New cash benefits program

Institute of Medicine 2003
We Can Do Better
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 GANDHII
“Never, ever, think outside the box.”