From Foundation Frameworks to Future Innovations to Future Generations:
A Call to Action

Michael C. Lu, MD, MPH
Associate Administrator
Maternal and Child Health
Health Resources and Services Administration
U.S. Department of Health and Human Services

11th Annual DHMIC Summit
Wilmington, DE

April 13, 2016
Life Course Perspective
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
Developmental Origins of Health & Disease
Barker Hypothesis
Birth Weight and Coronary Heart Disease

Barker Hypothesis
Birth Weight and Hypertension

Barker Hypothesis
Birth Weight and Insulin Resistance Syndrome

Maternal Stress & Fetal Programming

Hypothalamus → Pituitary → Adrenal → Placenta

CRH → ACTH → Cortisol → DHEA-S

Norepinephrine → 11-B HSD II
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

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

<table>
<thead>
<tr>
<th>Year</th>
<th>Black</th>
<th>Hispanic</th>
<th>White</th>
</tr>
</thead>
<tbody>
<tr>
<td>1976-1980</td>
<td>7.6%</td>
<td>6.2%</td>
<td>4.7%</td>
</tr>
<tr>
<td>1988-1994</td>
<td>11.6%</td>
<td>13.5%</td>
<td>9.3%</td>
</tr>
<tr>
<td>1999-2002</td>
<td>17.7%</td>
<td>19.2%</td>
<td>14.0%</td>
</tr>
</tbody>
</table>

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 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 MOCHE guidelines. The review included literature posted on PubMed and Medline and was published between January 1975 and December 2005. Prenatal exposures to maternal diabetes, malnutrition, and cigarette smoking were examined, and primary study outcomes were childhood overweight or obesity as measured by body mass index (BMI) for children ages 5 to 21.

Results: Four of six 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 1.0–1.8). 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 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 glucose transport 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 a window of opportunity for obesity prevention.

Keywords: Prenatal programming - Childhood obesity - Overweight - Developmental programming - Fetal programming - Maternal diabetes - 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 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. It is also associated with cognitive or intellectual impairments and social exclusion and stigmatization as parts of a vicious cycle including school avoidance [1]. Childhood obesity tracks strongly into adulthood [4, 5]; obesity beyond
Maternal Diabetes &
Intrauterine Hyperglycemia

Intrauterine Hyperinsulinemia (Fetal Pancreatic β Cells)

Preadipocyte Differentiation

Adipocyte Hyperplasia

Programmed Insulin Resistance

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

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

Births
- <32: 2%
- 32-33: 2%
- 34-36: 9%
- 37+: 87%

Infant Deaths
- <32: 54%
- 37+: 32%
- 34-36: 10%
- 32-33: 4%

Source: NCHS, linked birth/infant death data set
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.
From Foundation Frameworks to Future Innovations
to Future Generations
Closing the Black-White Gap in Birth Outcomes:
A 12-Point Plan

1. Provide interconception care to women with prior adverse pregnancy outcomes
2. Increase access to preconception care for African American women
3. Improve the quality of prenatal care
4. Expand healthcare access over the life course
5. Strengthen father involvement in African American families
6. Enhance service coordination and systems integration
7. Create reproductive social capital in African American communities
8. Invest in community building and urban renewal
9. Close the education gap
10. Reduce poverty among Black families
11. Support working mothers and families
12. Undo racism

Call to Action #1

Improve women’s health across the life course
Call to Action #2

Strengthen families and communities
Fatherhood
Where’s the F in MCH?

Barriers to Father Involvement

• Historical
  • Slavery
  • Deindustrialization
  • War on drugs, war on crimes

• Individual
  • Knowledge, attitude, behavior
  • Human capital: education, employment

• Interpersonal
  • Child’s mother
  • Child’s maternal grandmother

• Neighborhood & Community
  • Employment
  • Incarceration

• Policy
  • EITC
  • TANF
  • Child Support

• Life Course

Call to Action #3

Address social & economic inequities
Racism
MATERNAL LIFETIME EXPOSURE TO INTERPERSONAL RACISM IN 3 OR MORE DOMAINS AND INFANT BIRTH WEIGHT
(Collins et al, AJPH, 2004)

OR=2.7 (1.3-5.4)
Going Public

Levels of Racism: A Theoretic Framework and a Gardener’s Tale

Camarasa Patellas Jones, MD, MPH, PhD

Racism-associated differences in health outcomes are routinely documented in this country, yet for the most part they remain poorly explained. Indeed, rather than vigorously exploring the basis of these differences, many scientists either adjust for race or restrict their studies to race groups. Ignoring the etiologic factors embedded in group differences impedes the advance of scientific knowledge, limits efforts at primary prevention, and perpetuates ideas of biologically determined differences between the races.

The variable race is only a rough proxy for socioeconomic status, culture, and genetic, but it precisely captures the social classification of people in a race-conscious society such as the United States. The race noted on a health form is the same race noted by a sales clerk, a police officer, or a judge, and this racial classification has a profound impact on daily life experience in this country. This is the variable “race” is not a biological construct that reflects innate differences, but a social construct that precisely captures the impact of racism.

For this reason, some investigators now hypothesize that race-associated differences in health outcomes are in fact due to the effects of racism. In light of the Department of Health and Human Services Initiative to Eliminate Racial and Ethnic Disparities in Health by the Year 2010, it is important to be able to examine the potential effects of racism in causing race-associated differences in health outcomes.

Levels of Racism

Those developed a framework for understanding racism on 3 levels: institutionalized, personally mediated, and internalized. This framework is useful for raising new hypotheses about the basis of race-associated differences in health outcomes, as well as for designing effective interventions to eliminate those differences. In this framework, institutionalized racism is defined as differential access to the goods, services, and opportunities of society by race. Institutionalized racism is normative, sometimes legalized, and often manifest as inherited social privilege. It is structural, having been codified in our institutions of custom, practice, and law, so there need not be an identifiable perpetrator. Indeed, institutionalized racism is often evident as reaction to the face of need.

Institutionalized racism manifests itself both in material conditions and access to power. With regard to material conditions, examples include differential access to quality education, sound housing, gainful employment, appropriate medical facilities, and a clean environment. With regard to access to power, examples include differential access to information (including one’s own history, resources (including wealth and organizational infrastructure), and voice (including voting rights, representation in government, and control of the media). It is important to note that the association between socioeconomic status and race in the United States has its origins in discrete historical events but persists because of contemporary structural factors that perpetuate these historical injustices. In other words, it is because of institutionalized racism that there is an association between socioeconomic status and race in this country.

Personally mediated racism is defined as prejudice and discrimination, where prejudice includes differential assumptions about the abilities, motives, and intentions of others according to race.
Collective Impact
Collective Impact

- Common Agenda
- Shared measurement systems
- Mutually reinforcing activities
- Continuous communication
- Backbone support organizations
All this will not be finished in the first 100 days. Nor will it be finished in the first 1,000 days, nor in the life of this Administration, nor even perhaps in our lifetime on this planet. But let us begin.

John F Kennedy (1961)