Preconception Health & Health Care: A Life-Course Perspective

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What is Preconception Care?

- A set of interventions that aim to identify and modify biomedical, behavioral, and social risks to a woman's health or pregnancy outcome through prevention and management.
What Is Preconception Care?

- **Risk Assessment**
  - Reproductive life plan
  - Past pregnancy history
  - Past medical & surgical history
  - Medications & allergies
  - Family & genetic history
  - Social history
  - Behavioral & nutritional assessment
  - Mental health
  - Laboratory testing

- **Health Promotion**
  - Family planning
  - Stress resilience
  - Nutritional preparedness
  - Immune allostasis
  - Healthy environment

- **Medical & Psychosocial Interventions**
  - Individualized for identified risks
  - Preventive services and primary care

Recommendation 1. Individual responsibility across the life span. Each woman, man and couple should be encouraged to have a reproductive life plan.

Recommendation 2. Consumer awareness. Increase public awareness of the importance of preconception health behaviors and preconception care services by using information and tools appropriate across various ages; literacy, including health literacy; and cultural/linguistic contexts.

Recommendation 3. Preventive visits. As a part of primary care visits, provide risk assessment and educational and health promotion counseling to all women of childbearing age to reduce reproductive risks and improve pregnancy outcomes.

Recommendation 4. Interventions for identified risks. Increase the proportion of women who receive interventions as follow-up to preconception risk screening, focusing on high priority interventions (i.e. those with evidence of effectiveness and greatest potential impact).

Recommendation 5. Interconception care. Use the interconception period to provide additional intensive interventions to women who have had a previous pregnancy that ended in an adverse outcome (i.e., infant death, fetal loss, birth defects, low birthweight, or preterm birth).

Recommendation 6. Prepregnancy checkup. Offer, as a component of maternity care, one prepregnancy visit for couples and persons planning pregnancy.

Recommendation 7. Health insurance coverage for women with low incomes. Increase public and private health insurance coverage for women with low incomes to improve access to preventive women’s health and preconception and interconception care.

Recommendation 8. Public health programs and strategies. Integrate components of preconception health into existing local public health and related programs, including emphasis on interconception interventions for women with previous adverse outcomes.

Recommendation 9. Research. Increase the evidence base and promote the use of the evidence to improve preconception health.

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
- Preconception health & healthcare
Early Programming
Barker Hypothesis
Birth Weight and Coronary Heart Disease

Barker Hypothesis
Birth Weight and Insulin Resistance Syndrome

Odds ratio adjusted for BMI

Barker Hypothesis
Birth Weight and Insulin Resistance Syndrome

<table>
<thead>
<tr>
<th>Birth weight</th>
<th>&lt;5.5</th>
<th>5.6-6.5</th>
<th>6.6-7.5</th>
<th>7.6-8.5</th>
<th>8.6-9.5</th>
<th>&gt;9.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odds Ratio</td>
<td>18</td>
<td>8.4</td>
<td>8.5</td>
<td>4.9</td>
<td>2.2</td>
<td>1</td>
</tr>
</tbody>
</table>
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 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

1976-1980
1988-1994
1999-2002

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

Results: Of six included studies of prenatal exposure to maternal diabetes, five 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 cohort 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, and neuroendocrine responses 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 · Prenatal programming · Gestational diabetes · Maternal malnutrition · Cigarette smoking

Children overweight and obesity is a growing problem in the United States and worldwide. The prevalence of child- hood 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. 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
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
Sequelae of Preterm Birth

- Term Births: 12%
- Preterm Birth:
  - Perinatal Mortality: 75%
  - Neurologic Disabilities: 50%
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

African American: 18.4%
White: 11.7%

Year 2010 Goal: 8%

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

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).
Kaplan-Meier plots of cumulative probability of survival without admission or death from ischemic heart disease after first pregnancy in relation to preterm birth.
Preterm Birth &
Maternal Hypertension

Lu, et al. manuscript in preparation

![Graph showing survival over analysis time in days for different racial groups and preterm birth categories.](image)
Preconception Health and Health Care: A Life-Course Perspective
Preconception is a critical period for children’s health.
Early Prenatal Care Is Too Late

- To prevent some birth defects
- To prevent implantation errors
- To restore allostasis
Preconception is a critical period for children’s health

- Folic acid
- Rubella seronegativity
- Diabetes (preconception)
- Hypothyroidism
- HIV/AIDS
- Maternal phenylketonurea (PKU)
- Oral anticoagulant
- Antiepileptic drugs
- Isotretinoin (Accutane)
- Smoking
- Alcohol misuse
- Obesity
- STD
- Hepatitis B

Preconception Care for Men

- tobacco
- alcohol
- drugs (e.g. anabolic steroids)
- caffeine
- poor diet
- radiation and chemotherapy
- testicular hyperthermia
- diabetes mellitus
- varicoceles
- epididymitis
- 1,2-dibromo-3-chloropropane
- nonylphenol
- polycyclic aromatic hydrocarbons (PAHs)
- polychlorinated biphenyls (PCBs)
- dioxins
- phthalates

Early Prenatal Care Is Too Late

Implantation Errors

# The Role of the Placenta in Fetal Programming


## Table 1. Associations between placental weight and the placental weight/birthweight ratio (placental ratio) and long-term cardiovascular and metabolic outcomes

<table>
<thead>
<tr>
<th>Blood pressure</th>
<th>Association with later outcome</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small placental weight</td>
<td>↑ adult blood pressure</td>
<td>Campbell et al., 1996</td>
</tr>
<tr>
<td>Small placental weight</td>
<td>↑ adult hypertension with diabetes</td>
<td>Eriksson et al., 2000</td>
</tr>
<tr>
<td>Small placental volume</td>
<td>↑ childhood blood pressure</td>
<td>Thame et al., 2000</td>
</tr>
<tr>
<td>Large placental weight</td>
<td>↑ adult blood pressure</td>
<td>Barker et al., 1990</td>
</tr>
<tr>
<td>Large placental weight</td>
<td>↑ childhood blood pressure</td>
<td>Law et al., 1991</td>
</tr>
<tr>
<td>Large placental weight</td>
<td>↑ childhood blood pressure (boys only)</td>
<td>Moore et al., 1996</td>
</tr>
<tr>
<td>Large placental weight</td>
<td>↑ adult blood pressure</td>
<td>Taylor et al., 1997</td>
</tr>
<tr>
<td>High placental ratio</td>
<td>↑ adult blood pressure</td>
<td>Barker et al., 1992</td>
</tr>
<tr>
<td>High placental ratio</td>
<td>↑ adult hypertension without diabetes</td>
<td>Moore et al., 1999</td>
</tr>
<tr>
<td>High placental ratio</td>
<td>↑ adult blood pressure</td>
<td>Eriksson et al., 2000</td>
</tr>
<tr>
<td>Placental weight/ratio</td>
<td>↑ childhood blood pressure</td>
<td>Whincup et al., 1995</td>
</tr>
<tr>
<td>Placental weight/ratio</td>
<td>↑ adult blood pressure</td>
<td>Martyn et al., 1995b</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>↑ coronary heart disease (men)</td>
<td>Forsen et al., 1997</td>
</tr>
<tr>
<td>Placental weight</td>
<td>↑ coronary heart disease (men)</td>
<td>Martyn, Barker &amp; Osmond, 1996</td>
</tr>
<tr>
<td>Placental weight</td>
<td>↑ coronary heart disease (men &amp; women)</td>
<td>Leon et al., 1998</td>
</tr>
<tr>
<td>Placental weight</td>
<td>↑ coronary heart disease (women)</td>
<td>Forsen et al., 1999</td>
</tr>
<tr>
<td>Placental weight</td>
<td>↑ coronary heart disease (men)</td>
<td>Eriksson et al., 2001</td>
</tr>
<tr>
<td>Low placental ratio</td>
<td>↑ coronary heart disease (men)</td>
<td>Martyn, Barker &amp; Osmond, 1996</td>
</tr>
<tr>
<td>High placental ratio</td>
<td>↑ coronary heart disease (men)</td>
<td>Martyn, Barker &amp; Osmond, 1996</td>
</tr>
<tr>
<td>High placental ratio</td>
<td>↑ coronary heart disease (women)</td>
<td>Forsen et al., 1999</td>
</tr>
<tr>
<td>Stroke</td>
<td>↑ stroke death rates</td>
<td>Martyn, Barker &amp; Osmond, 1996</td>
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<tr>
<td>Glucose tolerance</td>
<td>↑ type-2 diabetes</td>
<td>Forsen et al., 2000</td>
</tr>
<tr>
<td>High placental ratio</td>
<td>↑ prevalence of impaired glucose tolerance</td>
<td>Phipps et al., 1993</td>
</tr>
<tr>
<td>Plasma fibrinogen</td>
<td>↑ plasma fibrinogen</td>
<td>Martyn et al., 1995a</td>
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<tr>
<td>Small placental weight</td>
<td>↑ plasma fibrinogen</td>
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</tr>
<tr>
<td>High placental ratio</td>
<td>↑ plasma fibrinogen</td>
<td></td>
</tr>
</tbody>
</table>

*↑ = association found in the direction shown; — = no significant association found. *Measured in mid-trimester.
Preconception care is no quick fix for women’s health.
Where is the A in MCH?
It take more than preconception care to promote preconception health

- Sustainable development
- Human development
- Economic development
- Community development
Preconception care is no silver bullet for disparities in birth outcomes.
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

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)