Developmental Origins of Health and Disease: Type 2 Diabetes

Rebecca Simmons, M.D.
Children’s Hospital of Philadelphia
Perelman School of Medicine University of Pennsylvania
IUGR
Aberrant Fetal Growth

Embryonic and Fetal Exposures

TIME Special Report
Inside The Womb

MATERNAL OBESITY
Edited by Matthew W. Gillman and Lucilla Poston

Gestational Diabetes
What to Expect

BPA

Aberrant Fetal Growth
What is the evidence for fetal programming?
Dutch Hunger Winter
Acute famine in the western Netherlands from October 1944-May 7, 1945.

Nazi imposed embargo on all incoming transport, including food.

Daily ration of 580 calories.

Ravelli et al, NEJM 1976
Prevalence of Type 2 Diabetes

Weight (kg)

Ponderal index (kg/m³)

Prevalence (%)
Barker Hypothesis

Fetal undernutrition “programs” cellular number and functional adaptations of organ and metabolic systems, resulting in increased susceptibility to adult diseases.

The Barker Hypothesis

Barker DJ. BMJ, 2003

Ethel Margaret Burnside
Nurse Midwife
Odds ratio for impaired glucose tolerance or type 2 diabetes according to birth weight among 370 men aged 64 years born in Hertfordshire

Monozygotic twins discordant for diabetes

<table>
<thead>
<tr>
<th></th>
<th>Diabetic</th>
<th>Nondiabetic</th>
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</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>67 ± 2</td>
<td>67 ± 2</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>83 ± 4*</td>
<td>72 ± 5</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>165 ± 3</td>
<td>164 ± 3</td>
</tr>
<tr>
<td>Waist/Hip ratio</td>
<td>0.95 ± 0.01*</td>
<td>0.91 ± 0.02</td>
</tr>
<tr>
<td>Birth weight</td>
<td>2634 ± 135*</td>
<td>2829 ± 131</td>
</tr>
</tbody>
</table>

Poulsen, Diabetologia 1997
Nurses Health Study

69,526 married female nurses 30-55 years of age in 1976.
Risk for Development of Type II Diabetes

<table>
<thead>
<tr>
<th>Birth weight (lbs)</th>
<th>Relative Risk</th>
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<tbody>
<tr>
<td>&lt; 5.5</td>
<td>1.0</td>
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<tr>
<td>5.5 - 6.9</td>
<td>1.5</td>
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<tr>
<td>7.0 - 8.4</td>
<td>2.0</td>
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<tr>
<td>8.5 - 10.0</td>
<td>1.5</td>
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<tr>
<td>&gt; 10.0</td>
<td>1.0</td>
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</tbody>
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referent
Male Health Professionals Follow-up Study

- 51,529 male dentists, optometrists, osteopaths, pharmacists, podiatrists, and veterinarians 40-75 years of age in 1986.

Curhan et al, Circulation, 1996
Risk for Development of Type II Diabetes

Relative Risk

Birth weight (lbs)

- <5.5
- 5.5-6.9
- 7.0-8.4
- 8.5-10.0
- >10.0

Referent
Small at Birth, Big at Eight Years, or Both?
The Role of Catch-up Growth
Insulin Resistance in 8-Year-Old Indian Children

Bavdekar A, Diabetes 1999
Relationship Between Birthweight and Insulin Resistance

(Adjusted for age, sex, and current body weight)

Light at Birth

OR: 1.48

Average at 8

OR: 1.6

Tall at 8

Heavy at 8

OR: 8.3
Relationship Between Parental Height and Insulin Resistance

Short Parents

Light at Birth

Tall & Heavy at 8

OR: 10.48
Principles of Programming

➢ There are critical periods of vulnerability which occur at different times for different tissues. Cells dividing rapidly are at greatest risk.

➢ Programming has permanent effects that alter responses in later life and can modify susceptibility to disease.

➢ Programming may involve structural changes in important organs.

➢ The effects of programming may be transferred across generations via epigenetic mechanisms.

➢ Programming is often gender specific.
WHY YOUR DNA ISN’T YOUR DESTINY

The new science of epigenetics reveals how the choices you make can change your genes — and those of your kids

BY JOHN CLOUD
DNA methylation: Methyl marks added on cytosine repress gene activity, heritable modification.
Can we prevent the development of diabetes and obesity?
Feeding the Small for Gestational Age Infant
Feeding the Small for Gestational Age Infant

What’s the right strategy?

- Infants born small-for-gestational age (SGA) are at higher risk for adult diseases.
- Metabolic and cardiovascular risk may be modulated by nutrition in early infancy.
Early adiposity rebound in childhood and risk of Ty2 diabetes in adult life

Fig. 1. Mean Z-scores for height, weight and BMI during childhood in 290 people who later developed Type 2 diabetes within a cohort of 8760 men and women. At any age, the mean Z-score for the cohort is set at 0 while the standard deviation is set at 1.
BREASTFEEDING

It Rocks!
Which Milk Should Be Fed to the SGA Infant?

Growth considerations

- The ideal postnatal growth rate for SGA infants is not known.

- A fetus grows in utero at a rate of at least 15-20 g/kg/day. To attain this rate, the SGA infant would need approximately 110-135 kcal/kg/day with additional energy for catch-up growth.
Catch up growth: is it good?

- Catch-up growth may need to be gradual: not too much and not too fast.

- If an infant is SGA at birth and subsequently has a discharge weight AGA, this represents early postnatal catch-up growth and may be a risk factor for metabolic syndrome in adult life.

- Healthy catch-up growth is paralleled by an increase in linear growth and lean body mass, and unhealthy catch-up growth is associated with an increase in fat mass, central adiposity, and insulin resistance.
Catch up growth: is it good?

- The slower the rate of intrauterine growth, the less likely the infant will exhibit catch-up growth.
- Less-affected and healthier SGA infants are more likely to respond to nutritional intervention and exhibit catch-up growth during the first 6 months.
- The lower the gestational age, the longer it takes to achieve final catch-up growth and the worse the long-term prognosis.
Catch-up Growth in Exclusively Breast fed SGA babies

- Growth occurs in sequence
- Normalization of lean mass occurs by 4 months of age
- Normalization of bone mineral content occurs by 12 months of age
- Fat mass still reduced at 12 months of age
Catch-up Growth in Formula Fed SGA babies

- Early catch up of fat mass
- Associated with elevated levels of IGF-1 and low levels of adiponectin (risk factors for later development of obesity and insulin resistance)
Summary

- Breast feeding is best
- Current feeding strategies may lead to the later development of metabolic syndrome, but the primary consideration is head growth
- More research is needed!