The First 1,000 Days + and Lifelong Health

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Proper nutrition and growth in utero and during early life are the foundation of adult health.

Poor childhood nutrition is associated with delayed growth, impaired cognitive development, adult chronic diseases, and lower income.

As well, maternal and paternal health prior to conception are major factors influencing offspring health.
Influences on Growth and Development

BIOLOGICAL
- Pre-conceptual health of parents
- Maternal diet in utero
- Complementary feeding
- Diverse microbiome

ENVIRONMENTAL
- Infectious diseases
- Environmental toxins

SOCIO-ECONOMIC
- Maternal education
- Exposure to ultra-processed foods
- Spontaneous physical activity
Timing of Interventions is Critical
Preimplantation Diet and Offspring Health

• Female rats fed low protein diet only during preimplantation

<table>
<thead>
<tr>
<th></th>
<th>18% casein</th>
<th>Male</th>
<th>9% casein</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure</td>
<td>90.29±2.28 (n=19)</td>
<td>102.32±3.49* (n=16)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(mmHg) at 4 weeks of age</td>
<td>106.16±2.01 (n=35)</td>
<td>115.39±3.33*(n=28)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>0.669±0.010 (n=36)</td>
<td>0.708±0.016* (n=31)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(mmHg) at 11 weeks of age</td>
<td>5.02±0.066 (n=36)</td>
<td>4.46±0.180* (n=31)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kidney/body weight (%)</td>
<td>0.25±0.004 (n=36)</td>
<td>0.26±0.008 (n=31)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver/body weight (%)</td>
<td>0.914±0.041 (n=36)</td>
<td>0.969±0.053 (n=31)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spleen/body weight (%)</td>
<td>0.398±0.007 (n=36)</td>
<td>0.423±0.021 (n=31)</td>
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</tr>
</tbody>
</table>

• LPD pups exhibited significant “catch-up” growth.
• Offspring of LPD dams had increase systolic blood pressure and disproportionate growth of specific organs.
Periconception and Offspring Health
Periconception and Offspring Health

- paternal obesity influences 2\textsuperscript{nd}, but not 3\textsuperscript{rd} generation offspring on high fat “Western” diet.
Periconception and Offspring Health

![Graph showing official daily government ration (kcal per day) and average temperature (°C) over time from Nov'44 to May'45.](image)

![Graph showing DNA methylation differences over time from Nov'44 to May'45.](image)
Epigenetics and Offspring Body Composition

- Methylation pattern of umbilical RXRA is associated with offspring adiposity.
Maternal Health and Offspring Health

- Current trend in Japan for women to limit gestational weight gain (GWG)
- Women with lower GWG had increased risk of low birth weight and SGA births
## Maternal Body Composition and Fetal Growth

<table>
<thead>
<tr>
<th>Variable</th>
<th>Unstandardized β coefficient</th>
<th>SE</th>
<th>Standardized β coefficient</th>
<th>p</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BWt</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constant</td>
<td>−452.02</td>
<td>93.97</td>
<td></td>
<td>&lt;0.001</td>
<td>0.21</td>
</tr>
<tr>
<td>FM (kg)</td>
<td>22.60</td>
<td>4.21</td>
<td>0.47</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td><strong>ΔEFW</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constant</td>
<td>1809.58</td>
<td>370.42</td>
<td></td>
<td>&lt;0.001</td>
<td>0.27</td>
</tr>
<tr>
<td>FM (kg)</td>
<td>18.39</td>
<td>8.34</td>
<td>0.33</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>FFM (kg)</td>
<td>20.07</td>
<td>9.56</td>
<td>0.31</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>−14.76</td>
<td>6.99</td>
<td>−0.24</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td><strong>Δ femur length</strong>^a^</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constant</td>
<td>−0.91</td>
<td>0.97</td>
<td></td>
<td>0.35</td>
<td>0.26</td>
</tr>
<tr>
<td>Maternal glucose (mg/dl)</td>
<td>0.72</td>
<td>0.21</td>
<td>0.47</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>Parity</td>
<td>0.11</td>
<td>0.05</td>
<td>0.29</td>
<td>0.04</td>
<td></td>
</tr>
</tbody>
</table>

BWt, birth weight adjusted for gestational age; ΔEFW, change in estimated foetal weight between second and third trimester of gestation.

^a^Rate of femur growth between second and third trimester of gestation.
Stunting and Obesity

• Size at birth and subsequent growth are primary predictors of adult size.

• Some studies reported an increased risk for obesity among adults who stunted as children. (Popkin et al 1995, Sichieri et al 2010)

• Studies from other regions have reported no association between stunting and obesity. (Cameron et al 2002, Walker et al 2002, and Corvalán et al 2007)
Growth Retardation and Metabolic Adaptations

- Impaired fat oxidation in growth retarded children and adults from diverse geographic regions.

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>Growth Retarded</th>
<th>Control</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil(^1)</td>
<td>(HAZ -2.16)</td>
<td>(HAZ 0.56)</td>
<td>0.01</td>
</tr>
<tr>
<td>Russia(^2)</td>
<td>(HAZ -3.00)</td>
<td>(HAZ -3.00)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Korea(^3)</td>
<td>(HAZ -0.90)</td>
<td>(HAZ 0.40)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Adapted from:
Stunting and Body Composition

- Stunting was not associated with increased adiposity, but difference in blood pressure was greater than normal height peers.
Early Growth and Adult Body Composition

- Persistent, rapid growth was associated with greater fat mass.
- Short duration of breastfeeding was associated with rapid growth classes.
## Growth Patterns and Body Composition

<table>
<thead>
<tr>
<th>Latent Class</th>
<th>Girls</th>
<th>Boys</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>$\beta = -0.17$</td>
<td>$\beta = -0.40$</td>
</tr>
<tr>
<td>Med</td>
<td>$\beta = -0.17$</td>
<td>$\beta = -0.40$</td>
</tr>
<tr>
<td>Low</td>
<td>$\beta = 0.69$</td>
<td>$\beta = 0.69$</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Girls</th>
<th>Boys</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\beta = 0.52$</td>
<td>$\beta = 0.54$</td>
</tr>
</tbody>
</table>

Independent of current body weight, SES, maternal education, and parity.

**UNPUBLISHED DATA**
Summary

• Time to consider the “First 1,000 Days +”
• Maternal diet and health remain important factors for fetal growth.
• Effective interventions may be easiest during pregnancy and infancy.
• Growth continues until adulthood and efforts to improve diet and activity remain important throughout childhood.
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