The Role of Disparity in the Origins of Obesity Risk

Linda S. Adair, PhD
Department of Nutrition
Gillings School of Global Public Health
University of North Carolina, Chapel Hill
Disparity...
A great difference
A lack of equality
Prevalence of obesity (BMI > 95th %ile of CDC growth reference), by age and race/ethnicity

Prevalence of overweight in children <5 yr, DHS data from 26 countries

WHO Weight-for length or height Z-score >2
The nature of disparities with important implications for child obesity:

**Resources**

- Inequities in health-promoting resources: SES factors (wealth, income, education, social status) relate to disparities in:
  - Nutrition: Food availability/food security, diet quality
  - Physical activity resources and environment
The nature of disparities with important implications for child obesity:

Exposures

• Inequities in pathogenic exposures
  – Environmental pollutants: air and water quality, pesticides
  – Microbial pathogens: sanitation and hygiene, water quality, close living quarters

• Differences in stress and social support
  – financial, physical, emotional, life events
What aspects of disparity does the developing fetus or young infant experience?

**Nutrition**

- Amount and balance of macro- and micronutrients which reflect:
  - Maternal STORES (e.g. adiposity)
  - Current dietary INTAKE (e.g. specific macro and micronutrients)
  - Maternal Metabolism (e.g. gestational diabetes, MTHFR genotype)
What aspects of disparity does the developing fetus or young infant experience?

- Toxins/environmental exposures
  - smoking-related
  - heavy metals
  - endocrine disruptors

- Hormones
  - Growth and metabolic hormones
    - Insulin, leptin
  - Stress hormones
    - Cortisol
Maternal nutrition-related pathways of risk for child obesity

**Maternal undernutrition:**

- Underweight (BMI < 18.5 kg/m\(^2\)), inadequate gestational weight gain, micronutrient inadequacies
  - Prevalent in LMIC, reflects SES and race/ethnicity disparity in higher income countries
  - Low prepregnancy BMI increases risk of
    - \(^1\)LBW by 47%
    - \(^1\)SGA by 81%
    - \(^2\)Preterm birth by 32%
  - Micronutrient deficiencies (iodine, zinc, iron) increase risk of LBW, SGA and/or preterm birth\(^3\)

2. Dean et al Reproductive Health 2014;11:s3-s15.
Maternal nutrition-related pathways of risk for child obesity

**Maternal excess nutrition**

- overweight (BMI > 25 kg/m²) excess gestational weight gain, dietary excesses
  - Maternal pre-pregnancy overweight increases risk of having a LGA infant by 53%¹
  - Maternal prepregnancy obesity doubles risk of LGA¹
  - Excess maternal weight gain increases macrosomia and LGA²

Maternal *Pre-pregnancy weight status*, by race/ethnicity

US Pregnancy and Perinatal Surveillance Data 2010
http://www.cdc.gov/pednss/
Maternal *pregnancy weight gain* by race/ethnicity

*US Pregnancy and Perinatal Surveillance Data 2010*

http://www.cdc.gov/pednss/
Global trends in thinness (BMI<18.5), overweight (BMI>25), and obesity BMI>30 in women of childbearing age. *Black RE et al Lancet. 2013 Aug 3;382(9890):427-5*
Maternal anemia, PIH, and GDM, by race/ethnicity

US Pregnancy and Perinatal Surveillance Data 2010
http://www.cdc.gov/pednss/
Global variation in infant outcomes

**Undernutrition**

- Latin America
- West & Central Africa
- East Africa
- Sub-Saharan Africa
- South Asia

- SGA
- LBW

**Macrosomia**

- Latin America
- Africa
- China
- South Asia

- BW > 4 kg

**References**

UNICEF State of the World’s Children 2015
Koyanagi et al. Lancet 2013;381:476-83
US differences in **adverse birth outcomes**, by race/ethnicity, 2011

US Pregnancy and Perinatal Surveillance Data 2010
http://www.cdc.gov/pednss/

- **Preterm**
- **>4 kg**
- **<2.5 kg**

**Multiple Races**

**Asian/Pacific Islander**

**American Indian/Alaska Native**

**Hispanic**

**Non-Hispanic Black**

**Non-Hispanic White**
Differences in postnatal growth

Data from the Early Childhood Longitudinal Study Birth Cohort US 2001-2007, n=4950

- Odds of overweight diverge according to SES at about 9 mo
- OW associated with SES in whites, Hispanics and Asians

Jones-Smith et al PLOS ONE 2014;9 (6) e100181
SES disparities in Prevalence of stunting (HAZ < –2 ) and overweight (BMI Z > 2 ) among children <5 in highest and lowest wealth quintiles in selected countries.

Red circles are lowest wealth quintiles, blue circles are highest wealth quintiles.

The burden of overweight is shifting to the poor in low and middle income countries

• In high income countries, obesity prevalence is higher in disadvantaged groups
• In LMIC ... historically, obesity was found mainly in upper SES groups, but is now increasing faster among lower income groups
Higher wealth groups had higher overweight prevalence across most LMICs, but some countries had faster increases in overweight among the lowest wealth quintile, resulting in an increasing burden of overweight among the poor in LMICs. Data from 39 LMICs 1991-2008, women 15-49 DHS

A positive difference in prevalence growth rates indicated the lowest wealth quintile had a higher rate of prevalence growth rate than did the highest quintile. Data from 39 LMICs 1991-2008, women 15-49 DHS

US race/ethnic differences in breastfeeding

Initiated Breastfeeding

Multiple Races
Asian/Pacific Islander
American Indian/Alaska Native
Hispanic
Non-Hispanic Black
Non-Hispanic White

Breastfeeding initiation and duration in low income US women (<200 poverty) Williams, Urban Institute WIC study

<table>
<thead>
<tr>
<th></th>
<th>Initiated BF</th>
<th>Ave. Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non Hisp White</td>
<td>54.3</td>
<td>4.4</td>
</tr>
<tr>
<td>AA</td>
<td>42.7</td>
<td>3.8</td>
</tr>
<tr>
<td>Hispanic</td>
<td>75.3</td>
<td>5.7</td>
</tr>
</tbody>
</table>
Variation in infant and toddler feeding

- Multiple aspects of infant and child feeding vary widely by maternal age, income, education, ethnicity and weight status
  - Initiation and duration of BF
  - Timing of introduction of complementary foods
  - Types of complementary foods:
    - fruits and vegetables, sweetened beverages, salty snacks

Feeding Infants and Toddlers, Nationally representative US sample
Hendricks et al J Am Diet Assoc 2006; 106(suppl 1:S135-48)
Social and economic disparities translate to obesity and health disparities via epigenetic mechanisms

<table>
<thead>
<tr>
<th>Disparity</th>
<th>Response</th>
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</table>
| Maternal glycemia during pregnancy | • Alters ADIPQ methylation profile in placenta (Bouchard et al 2012)  
• Differential methylation of genes in metabolic pathways (Ruchat et al 2013)  
• GDM associated with decreased methylation of MEST, NR3CI in cord blood and placenta (El Hajj et al 2013) |
| Parental overweight              | • Parental obesity associated with IGF2 hypomethylation at imprinted genes Soubry 2013)  
• Paternal obesity affects methylation (Soubry et al BMC Med 2013)   |
| Maternal diet                    | • Low CHO intake in early pregnancy associated with higher methylation of RXRA (Godfrey et al 2011)  
• Famine conditions affect IL10, leptin methylation (Tobi et al 2009)  
• Increased maternal B12 during pregnancy associated with decreased global DNA methylation in newborns  
• Increased infant B12 associate with reduced methylation of IGFBP3 (McKay et al PLoS One 2102 7, e33290) |
Social and economic disparities translate to obesity and health disparities via epigenetic mechanisms

<table>
<thead>
<tr>
<th>Disparity</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stress</td>
<td>Adverse childhood experiences related to methylation differences in genes that regulate the stress response among Native Americans (Brockie, Heinselmann and Gill, 2013)</td>
</tr>
<tr>
<td>Environmental Exposures, e.g. arsenic</td>
<td>Wide range of effects on DNA methylation, reviewed in Marsit CJ, J Exp Biol 2015;218:71-79</td>
</tr>
<tr>
<td>Maternal Depression</td>
<td>Depression associated with higher methylation of neauron GR, NR3CI and higher stress reactivity in offspring (Oberlander et al 2008)</td>
</tr>
<tr>
<td>Breastfeeding</td>
<td>Specific breast milk components shown to influence gene expression (lactoferrin, prostaglandin J, oligosaccharides) (Verducci et al Nutrients 2014; 6:1711-24)</td>
</tr>
</tbody>
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IMPLICATIONS
Adaptation and mismatch

• Epigenetic changes are examples of *developmental plasticity*. Adaptations that enhance survival in the environment to which the organism is exposed (with information about the environment communicated by maternal signals).

• Responses are also hypothesized to be *anticipatory*, i.e. well suited for future environments that have similar levels of key exposures (e.g. nutritional adequacy).

*Bateson, Gluckman and Hanson 2014; J Physiol 11:2357-2368*
Poor maternal diet, inadequate nutrient stores, placental factors, 

Organ-specific structural deficits, altered body composition, altered metabolism, altered regulatory mechanisms EPIGENETIC changes 

Dietary adequacy or excess, sedentary behavior, other environmental factors 

Fetal Nutritional Insufficiency 

Increased risk of obesity, chronic disease
Offspring of malnourished Indian mothers have deficits in lean body mass but not body fat.

White Caucasian, 3500 g
- Other 50%
- Muscle 20%
- Viscera 20%

Indian, 2700 g
- Other 60%
- Muscle 10%
- Viscera 10%

## India: An illustration of mismatch

Consider women now having babies (age 20-30 y)

### Conditions around the time of their birth

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
<th>Source</th>
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<tbody>
<tr>
<td>LBW</td>
<td>30%</td>
<td>1992 NFSH</td>
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<tr>
<td>Stunting (under age 3)</td>
<td>47%</td>
<td>WHO Global database</td>
</tr>
<tr>
<td>Under 5 mortality</td>
<td>118/1000</td>
<td>1990, UNICEF</td>
</tr>
<tr>
<td>TFR</td>
<td>2.3</td>
<td>1990, UNICEF</td>
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### Current Conditions

<table>
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<tr>
<th>Condition</th>
<th>Percentage</th>
<th>Source</th>
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<tbody>
<tr>
<td>BMI&gt;25</td>
<td>8.2%, women 20-29</td>
<td>2006 NFSH</td>
</tr>
<tr>
<td></td>
<td>17.4%, women 30-39</td>
<td></td>
</tr>
<tr>
<td></td>
<td>23.5% urban women</td>
<td></td>
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<tr>
<td>Obese, IOTF</td>
<td>11-12%</td>
<td>11-12%, New Delhi youth, 14-17 y</td>
</tr>
<tr>
<td>Central obesity</td>
<td>~25%</td>
<td>~25% of adult women</td>
</tr>
<tr>
<td>Diabetes</td>
<td>9-10%</td>
<td>9-10% Delhi &amp; Chennai</td>
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Mismatch and child obesity?

- Most studies of mismatch have focused on longer term effects
- Can mismatch help us understand rapid *infant* weight gain?
“Maternal Constraint”

• Birth weight is lower in infants born to first-time mothers, but... firstborns who are well-fed experience rapid postnatal weight gain

• Maternal prenatal environment prepared them for a lower plane of nutrition, but postnatal nutrition is not constrained
LBW and later overweight

Overweight at age 2-3 according to BW status

- LBW
- Overweight age 2-3
- Overweight young adult
An example of mismatch?

- LBW is associated with reduced risk of overweight at age 2-3 yr, but...
- Association is modified in firstborn infants
  - Firstborns LBW infants gained more weight than higher birth order LBW infants (0.3 - 0.4 kg) and were twice as likely as LBW infants of higher birth order to be overweight at age 2 yr (OR=2.04, 1.00-4.14)
Summary and conclusions

• Wide disparities in SES, physical environment, psychosocial factors and stress contribute to substantial differences in fetal exposure to nutrients, toxins, hormones, and other regulatory substances

• These disparities may affect fetal and infant growth and susceptibility to later obesogenic factors through EPIGENETIC and other pathways

• Elevated risk of child obesity may result from prenatal undernutrition as well as nutritional excesses
Summary and conclusions

• Risk may be greatest when the fetus is adapted to a maternal environment that differs from the environment faced as an infant and young child.

• Understanding the exact nature of pathways of risk may lead to interventions to eliminate the adverse effects of health disparities.