Maternal Obesity in Pregnancy; short and long-term effects on the offspring

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Grand Rounds
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UTHSCSA
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Disclosures

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Learning Objectives

Obesity: maternal, children, neonates
Maternal obesity and fetal growth
Gestational weight gain
Why lifestyle interventions during pregnancy have not improved perinatal outcomes

Prevalence of Obesity by Race/Ethnicity in Women of Reproductive Age (1999-2010)

<table>
<thead>
<tr>
<th>Body Mass Index ≥ 30</th>
<th>All Race/Ethnicity Groups</th>
<th>Non-Hispanic White</th>
<th>Non-Hispanic Black</th>
<th>Hispanic</th>
<th>Mexican American</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-39y</td>
<td>31.5 (26.8-35.5)</td>
<td>25.9 (22.3-31.3)</td>
<td>46.2 (44.3-67.5)</td>
<td>34.4 (30.9-38.2)</td>
<td>37.8 (33.2-42.7)</td>
</tr>
<tr>
<td>Body Mass Index ≥ 25</td>
<td>55.0 (51.3-58.8)</td>
<td>50.2 (47.7-52.8)</td>
<td>74.3 (71.1-77.6)</td>
<td>65.4 (61.2-70.5)</td>
<td>68.5 (64.8-72.9)</td>
</tr>
</tbody>
</table>

Flegal, JAMA; 2012

Prevalence of Obesity (BMI > 95%) by Race/Ethnicity in Children and Adolescents from 2-19 Years (2011-2014)

<table>
<thead>
<tr>
<th>Age Group</th>
<th>All Race/Ethnicity Groups</th>
<th>Non-Hispanic Asian</th>
<th>Non-Hispanic White</th>
<th>Non-Hispanic Black</th>
<th>Non-Hispanic Hispanic</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-5y</td>
<td>17.0 (15.5-18.5)</td>
<td>17.2 (15.8-18.7)</td>
<td>17.6 (16.2-19.2)</td>
<td>17.5 (16.0-19.0)</td>
<td>20.5 (19.0-22.0)</td>
</tr>
<tr>
<td>6-11y</td>
<td>10.0 (9.4-10.6)</td>
<td>10.0 (9.4-10.6)</td>
<td>10.0 (9.4-10.6)</td>
<td>10.0 (9.4-10.6)</td>
<td>13.5 (12.9-14.1)</td>
</tr>
<tr>
<td>12-19y</td>
<td>10.0 (9.4-10.6)</td>
<td>10.0 (9.4-10.6)</td>
<td>10.0 (9.4-10.6)</td>
<td>10.0 (9.4-10.6)</td>
<td>13.5 (12.9-14.1)</td>
</tr>
</tbody>
</table>

Ogden, JAMA; 2012

Age-adjusted Prevalence% (and 95% CI) of Obesity (BMI ≥ 30) and Class 3 Obesity (BMI ≥ 40), Female Sex and Survey Years, NHANES 2005-2014

<table>
<thead>
<tr>
<th>Year Group</th>
<th>Obesity (BMI ≥ 30)</th>
<th>Class 3 Obesity (BMI ≥ 40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005-6</td>
<td>35.3 (32.4-38.4)</td>
<td>7.4 (5.9-9.1)</td>
</tr>
<tr>
<td>2007-8</td>
<td>35.4 (33.1-37.8)</td>
<td>7.3 (6.2-8.5)</td>
</tr>
<tr>
<td>2009-10</td>
<td>35.8 (34.0-37.7)</td>
<td>8.1 (7.1-9.2)</td>
</tr>
<tr>
<td>2011-12</td>
<td>36.1 (32.6-39.9)</td>
<td>8.3 (6.9-9.8)</td>
</tr>
<tr>
<td>2013-14</td>
<td>40.4 (37.5-43.3)</td>
<td>9.9 (8.1-12.1)</td>
</tr>
</tbody>
</table>

Flegal, JAMA; 2012

Prevalence of Obesity (BMI > 95%) by Race/Ethnicity in Children and Adolescents from 2-19 Years (2011-2014)

<table>
<thead>
<tr>
<th>Year Group</th>
<th>Obesity (BMI &gt; 95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005-6</td>
<td>17.0 (15.5-18.5)</td>
</tr>
<tr>
<td>2007-8</td>
<td>17.2 (15.8-18.7)</td>
</tr>
<tr>
<td>2009-10</td>
<td>17.6 (16.2-19.2)</td>
</tr>
<tr>
<td>2011-12</td>
<td>17.5 (16.0-19.0)</td>
</tr>
<tr>
<td>2013-14</td>
<td>17.7 (17.0-18.5)</td>
</tr>
</tbody>
</table>

Flegal, JAMA; 2012
**Increase in Term Birth Weight 1975-2004**

*MetroHealth (Cleveland, OH)*

*Catalano, Obstet Gynecol; 2007*

**Maternal BMI**

*Gibson; BMC Pregnancy and Childbirth, 2015*

**Ethnicity and Race**

*Gibson; BMC Pregnancy and Childbirth, 2015*

**Gestational Age**

*Gibson; BMC Pregnancy and Childbirth, 2015*

**Ponderal Index**

*Gibson, BMC Pregnancy & Childbirth; 2015*
Learning Objectives

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Regulation of Fetal Body Composition

Fat Free Mass / Lean Body Mass
Genetic
Fat Mass
Intrauterine Environment

Birth Weight and Lean Body Mass

Catalano, unpublished

Birth Weight and Fat Mass

Catalano, unpublished

Maximum, Minimum, and Interquartile Ranges of Percent Body Fat in SGA, AGA, and LGA Neonates

Springel, SRI, 2015
**Body Composition in Neonates**

<table>
<thead>
<tr>
<th></th>
<th>GDM (n = 195)</th>
<th>NGT (n = 220)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth Weight (g)</td>
<td>3398 ± 550</td>
<td>3337 ± 549</td>
<td>ns</td>
</tr>
<tr>
<td>Lean body mass (g)</td>
<td>2962 ± 405</td>
<td>2973 ± 408</td>
<td>ns</td>
</tr>
<tr>
<td>Fat mass (g)</td>
<td>436 ± 206</td>
<td>382 ± 186</td>
<td>0.0002</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>12.4 ± 4.6</td>
<td>10.4 ± 4.6</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

**Factors Relating to Fetal Adiposity at Birth**

220 Normal Glucose Tolerance and 195 GDM

<table>
<thead>
<tr>
<th></th>
<th>r²</th>
<th>Δr²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fat Mass</td>
<td>0.066</td>
<td>-</td>
</tr>
<tr>
<td>EGA</td>
<td>0.136</td>
<td>0.070</td>
</tr>
<tr>
<td>Wt. Gain</td>
<td>0.171</td>
<td>0.035</td>
</tr>
<tr>
<td>Group (GDM)</td>
<td>0.187</td>
<td>0.016</td>
</tr>
</tbody>
</table>

% Neonatal Body Fat

<table>
<thead>
<tr>
<th></th>
<th>Pre-gravid BMI</th>
<th>EGA</th>
<th>Group (GDM)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.072</td>
<td>-</td>
<td>0.016</td>
</tr>
</tbody>
</table>

**Neonatal % Adiposity and Maternal BMI**

<table>
<thead>
<tr>
<th>Body Mass Index (kg/m²)</th>
<th>&lt;22.6</th>
<th>22.6-28.4</th>
<th>28.5-32.9</th>
<th>33.0-37.4</th>
<th>37.5-41.9</th>
<th>≥42.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent Fat &gt; 90%</td>
<td>0</td>
<td>4</td>
<td>12</td>
<td>18</td>
<td>20</td>
<td>20</td>
</tr>
</tbody>
</table>

**Neonatal Insulin Resistance at Birth**

Catalano, BJOG; 2003

**Adiposity at Birth Correlates with Adiposity in Children at Age 8**

Catalano; AJCN, 2009

**Insulin Resistance and Adiposity at Birth**

Catalano; Diabetes Care, 2009
**Learning Objectives**

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**IOM Gestational Weight Gain Guidelines (2009)**

- Underweight (18.5) 12.5 - 18 kg
- Normal weight (18.5-24.9) 11.5 - 16 kg
- Overweight (25.0-29.9) 7 – 11.5 kg
- Obese (> 30) 5 – 9 kg

**Prevalence of GWG Adequacy by Pre-Pregnancy BMI**

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**Changes in Lean Body Mass per IOM GWG**

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**Weighted Mean Difference between Women with Excess GWG and Women with Adequate GWG at: <1 year, =1 year to 9 years, and ≥15 years.**

Mannan, Nutr Rev; 2013

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**Odds Ratios of Child Outcomes for Newborn Sum of Skinfolds Higher by 1mm Overweight/obesity**

**Sum of skinfolds > 85th percentile**

Waist circumference - iliac > 85th percentile

Body fat percentage > 85th percentile

**OR (95% CI)**

Model 3 (excluding maternal BMI)

Model 4 (including maternal BMI)

1.04 (1.02-1.07) p=0.002

1.06 (1.03-1.09) p<0.001

1.05 (1.02-1.08) p=0.004

1.07 (1.04-1.10) p=0.058

1.05 (1.02-1.08) p=0.003

1.06 (1.03-1.09) p=0.009

HAPPO-FUS, ADA; 2017
Learning Objectives

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Changes in Fat Mass per IOM GWG

Gestational Weight Gain (kg) with Dietary and Lifestyle Interventions in Pregnancy

Waters, JCEM; 2012

Interpretation: A behavioural intervention addressing diet and physical activity in women with obesity during pregnancy is not adequate to prevent gestational diabetes, or to reduce the incidence of large-for-gestational-age infants.
Placental Developmental Changes in Insulin Receptor Location

First trimester

Maternal side: trophoblast cells

Third trimester

Fetal side: vascular endothelium


Insulin Response OGTT

Insulin Response (IVGTT) and Placental Weight

Insulin Response (IVGTT) and Neonatal Adiposity

At 20 Weeks Insulin Response Correlates with Ultrasound Estimates of Placental Volume

O'Tierney-Ginn, JCEM; 2015
Maternal-Placental Crosstalk and Fetal Growth

Principal Component analysis (PCA) of Placental Transcriptome

In vivo IR

Number of Regulated Genes by High IR (↑ insulin) in vivo

Main Biological Processes downregulated by high IR (↑ insulin) in vivo

Identification of early transcriptome signatures in placenta exposed to insulin and obesity

Global biological pattern after ClueGo - Cytoscape analysis.

Obesity-induced downregulation of the mitochondrial translocator protein (TSP1) impairs placental steroid production
Subject Demographics

<table>
<thead>
<tr>
<th>Maternal</th>
<th>Maternal</th>
<th>Maternal</th>
<th>Lactate</th>
<th>Insulin</th>
<th>Glucose</th>
<th>HOMA-IR</th>
<th>Plasma Estriol</th>
<th>Plasma Progesterone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: 31±5</td>
<td>Age: 31±5</td>
<td>Age: 31±5</td>
<td>7.1±1.4</td>
<td>6.1±1.4</td>
<td>106±15</td>
<td>0.3±0.1</td>
<td>1055±57</td>
<td>92±10</td>
</tr>
<tr>
<td>BMI: 30±6</td>
<td>BMI: 30±6</td>
<td>BMI: 30±6</td>
<td>106±15</td>
<td>0.3±0.1</td>
<td>1055±57</td>
<td>92±10</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(All values expressed as mean ± SD)

Plasma Estriol and Progesterone Concentrations in Lean and Obese Women

Cholesterol Concentrations in Maternal and Cord Plasma in Lean and Obese Women

Expression of Placental Cholesterol Transporters and Mitochondrial Biogenesis

Placental Lipid Content in Lean and Obese Women
Placental Lipid Content in Lean and Obese Women

Proposed Mechanism of Placental Lipid Metabolism in Obese Women

Does Pregnancy have a long-lasting Effect on a Women’s Metabolism?

or

is it Postpartum Weight Retention?

Insulin Response and Sensitivity Preconception, Pregnancy, and Postpartum

Resting Metabolic Rate, CHO and Fat Oxidation Preconception, Pregnancy, and Postpartum
Basal Endogenous Glucose Production Preconception, Pregnancy, and Postpartum

Body composition Preconception, Pregnancy, and Postpartum

Impact of Inter-Pregnancy Weight Change on LGA Infants

Arun, AJOG; 2013

Berggren, Diabetologia; 2015

NICHD HD-22965-19, HD-057236, CTSA-UL-1 RR-024989, ADA Diabetes Association of Greater Cleveland