EXCESSIVE MATERNAL WEIGHT GAIN DURING GESTATION LEADS TO OFFSPRING WITH INCREASED ADIPOGENIC POTENTIAL IN THE IMMEDIATE PERINATAL PERIOD IN PIGS

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Gestational weight gain in the U.S.

- Institute of Medicine recommendations

<table>
<thead>
<tr>
<th>Prepregnancy BMI</th>
<th>Total Weight Gain</th>
<th>Recommended GWG decreases with increasing prepregnancy BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight (&lt; 18.5 kg/m²)</td>
<td>12.5-18</td>
<td></td>
</tr>
<tr>
<td>Normal weight (18.5-24.9 kg/m²)</td>
<td>11.5-16</td>
<td></td>
</tr>
<tr>
<td>Overweight (25.0-29.9 kg/m²)</td>
<td>7-11.5</td>
<td></td>
</tr>
<tr>
<td>Obese (≥ 30.0 kg/m²)</td>
<td>5-9</td>
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</table>

- Approximately 20% of all pregnancies in the US gain more than the recommended amount of weight. Overweight and obese women are at particular risk.
- Excess weight gain presents health risks for both mother and offspring.
Pig Model

- Pig model serves as a good bridge between mouse and humans
- Studies in mice can be replicated in pigs
Perinatal Nutrition in Pigs

Piglet diet before weaning can be manipulated to cause maximum epigenetic effects during the perinatal period.
Study hypotheses

Hypothesis 1: Excessive weight gain during pregnancy due to increased energy intake will result in programming modifications that predispose offspring to obesity and aspects of the metabolic syndrome.

Hypothesis 2: Early postnatal nutrition has the ability to reverse or enhance the effect of maternal diet.
**Maternal Diets:**
m-Control: chow gestation diet
M-HE: high energy gestation diet
- Increased energy intake (kcal) by ~50%
- Matched for protein intake (g/day)

**Post-weaning Diets:**
Control: chow piglet diets
HE: high fat piglet diets
- Increased fat content of diet by 10-15%
Experimental methods for determining programming of offspring

- Birth
- Suckling period
- Weaning: assigned to post-weaning (Pwn) diet
- Growth phase (9 weeks): Weights measured every 1-2 weeks
- 12 weeks

- Adipose, Liver & intestine mRNA for transcript analysis
- Serum for glucose, insulin and NEFA analysis
High energy diet increased maternal weight gain and adiposity during gestation

*P<0.05
Offspring from sows fed a HE diet weighed more at 8 and 10 weeks of age.

<table>
<thead>
<tr>
<th>Main effect</th>
<th>P-value</th>
</tr>
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<tbody>
<tr>
<td>Mat</td>
<td>0.12</td>
</tr>
<tr>
<td>Pwn</td>
<td>0.93</td>
</tr>
<tr>
<td>Mat*Pwn</td>
<td>0.85</td>
</tr>
<tr>
<td>Day</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Mat<em>Pwn</em>Day</td>
<td>0.95</td>
</tr>
</tbody>
</table>

Increased childhood adiposity

![Graph showing weight gain over weeks with different diet groups (mNEwNE, mNEwHE, mHEwNE, mHEwHE). The graph indicates a significant difference in weight gain between the groups, with m-NE showing increased adiposity compared to m-HE.]
Feeding a HF diet to offspring from HF diet fed sows induced disturbed offspring glucose homeostasis

Maternal Diet

<table>
<thead>
<tr>
<th></th>
<th>M-Control</th>
<th>M-HE</th>
<th>P-Values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>p-Control</td>
<td>p-HE</td>
<td></td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>70</td>
<td>80</td>
<td>64</td>
</tr>
<tr>
<td>Insulin (ng/ml)</td>
<td>0.016</td>
<td>0.013</td>
<td>0.010</td>
</tr>
<tr>
<td>NEFA (mmol/L)</td>
<td>0.43</td>
<td>0.43</td>
<td>0.62</td>
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</tbody>
</table>

† Significantly different (P<0.05) from control group of the maternal group (mHE→wNE)
* Significantly different (P<0.05) from offspring of control dams fed the same post-weaning diet (mNE→wHE)
Adipose CEBPα and PPARγ at 48 hr
Adipose SFRP2 at 48hr
Adipose SFRP4 and SFRP5 at 3 wks

![Graph showing comparison of SFRP4 and SFRP5 levels between HE and Control groups.](image)
Adipose CEBPα and PPARγ at 3 wks
At 3 Months

- BW (kg)
  - M HE
  - M Control

- Back Fat (mm)
  - M HE
  - M Control

- BW (kg)
  - P HE
  - P Control

- Back Fat (mm)
  - P HE
  - P Control

P = 0.14
Adipose SFRP5 at 3 Mon
Adipose PPARγ at 3 Mon
Adipose CEBPα at 3 Mon
Summary

- Offspring of mothers that gained excess weight during pregnancy:
  - Weighed more at 8 weeks and 10 weeks of age, although were not significantly different at the end of the study.
  - Had higher expression of increased adipogenesis at 48 hr (SFRP2) and 3 wks (CEBPα, PPARγ, SFRP4, and SFRP5).
  - These indicators were lost at 12 wks.

- Pigs were still relatively young at sacrifice, so this might not be a good time to see the final effect of fetal programming in pigs.

- Postnatal diet might play a more dominant role in the determination of offspring adiposity in pigs.
Questions?
Relative abundance of liver transcripts at 12 wks

Early life metabolic & growth adaptations

Arentsen et al., 2014 Nutrition Research (In Press)
<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Control</th>
<th>High Energy</th>
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</thead>
<tbody>
<tr>
<td>Total intake, kg/day</td>
<td>2.05</td>
<td>3.0</td>
</tr>
<tr>
<td>Total Protein, g/day</td>
<td>370</td>
<td>395</td>
</tr>
<tr>
<td>Total Lysine, g/day</td>
<td>16.03</td>
<td>15.8</td>
</tr>
<tr>
<td>Total Fat, g/day</td>
<td>119</td>
<td>178</td>
</tr>
<tr>
<td>Metabolizable Energy, kcal/day</td>
<td>6761</td>
<td>10144</td>
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