Maternal Weight Gain: Developmental Programming Determinants of Adult Disease

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Optimal Weight Gain in 120,170 USA Obese Women

Class 1 Obese Women (BMI 30.0-34.9kg/m$^2$), 10-25lb

Class II Obese Women (BMI 35.0-39.9Kg/m$^2$), 0-9lb

Class III Obese Women (BMI 40kg/m$^2$ or more) Weight LOSS 0-9lb.

*Kiel et al, Obstet Gynecol 2007; 110; 752-8*
<table>
<thead>
<tr>
<th>Authors</th>
<th>Reduction in Weight Gain</th>
<th>No Reduction in Weight Gain</th>
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<td>Borberg et al, 1980</td>
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<td>Widga et al, 1999</td>
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<td>Gray Donald et al, 2000</td>
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<td>Olson et al, 2004</td>
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<td>Polley et al, 2002</td>
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<td>Kinnunen et al, 2007</td>
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<td>Wolff et al, 2008</td>
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<td>Claessson et al, 2007</td>
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Lower Weight Gain Associated With Reduced Insulin and Leptin

The child of the obese woman; ‘programmed’ for obesity in later life?
Congratulations; its an obesity time bomb!
Birthweight in the UK is rising

Birthweight 1983-2000
National statistics UK
The Obese Child is Likely to become a Fat Adult

High normal weight status in childhood predicts overweight in adulthood
Field, Cook & Gillman
*Obesity Research* 2005
Is maternal fatness linked to childhood fat mass?

• Principal component analysis of newborn body composition; maternal (but not paternal) fat is an independent determinant of neonatal fat (Shields et al, 2006)

• Maternal but not paternal fat mass independently related to neonatal fat mass (Harvey et al, 2007)

• Maternal exercise associated with reduced neonatal fat mass (Harvey et al, 2007)

• Maternal but not paternal fatness independently associated with childhood fatness at age 9 years (Gale et al, 2007)
What about Maternal *Weight Gain* and Childhood Obesity?
Pregnancy weight gain and childhood adiposity

- Weight gain associated with fat mass at 3 yrs (Oken et al, 2007)

- Weight gain *not* associated with fat mass at 9 years (Gale et al, 2007)
Pregnancy Weight Gain and Childhood Left Ventricular Mass/Growth
(Generation R study, Netherlands)

Maternal anthropometry and echocardiography of Left Ventricular Mass; 791 mothers and children (6 wk-6mths)

**Maternal Wt gain v Longitudinal LV Growth**

<table>
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<tr>
<th>Wt Gain (Kg)</th>
<th>Longitudinal LV Growth</th>
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<td>&lt;6.5</td>
<td>Reference</td>
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<td>6.5-9.0</td>
<td>-0.28 (-0.72, 0.17)</td>
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<td>≥9.0</td>
<td>0.46 (0.02,0.90)**</td>
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*Geelhoed et al, Pediatric Research 2008*
Animal Studies

Most have not directly addressed hypothesis of weight GAIN in pregnancy.
Maternal undernutrition

Reduction in litter size = neonatal overfeeding

Maternal overnutrition

Diabetes in pregnancy

Fat Adult Offspring

Fat rich maternal diet / cafeteria diet

Maternal energy rich diet; obesity prone rat
Maternal/neonatal dietary intervention

Animals Reared on Normal Diet

Phenotypic characteristics determined in adulthood

control
DIET-INDUCED OBESITY

- Control diet
- Highly palatable diet (20%FAT+sweetened condensed milk)

Mating
- 6 week Gestation & Lactation

DAMS (C57BL/6 mice)

Body weight and food intake

OFFSPRING
- 3 months
Weight Gain and Calorific Intake in Pregnant Mice Fed Fat/Sugar Rich Diet

Samuelsson et al, Hypertension 2008
Maternal Diet Obesity in C57BL/6J Mouse Leads to Increase in Offspring Abdominal Fat Mass

A. Dam

B. Adult offspring

B. Dam Fat pad mass

Inguinal Fat Pad Mass

**Figure:**

- **Control Dam** vs **Obese Dam**
- **Control Dam** vs **Obese Dam**

**Graphs:**

- **WAT mass (g)**
  - **Pregnancy**
  - **Weaning**

- **WAT weight (g)**
  - **Male**
    - **3 months**
    - **6 months**
  - **Female**
    - **3 months**
    - **6 months**

**Statistical Symbols:**

- ***
- **
- *
Maternal Obesity Programmes Offspring Appetite

Samuelsson et al, Hypertension 2008
Larger and Morphologically Abnormal Hearts in 28 day old Offspring of Obese mice

F Histological sections prepared by standard techniques (H&E) of neonatal mouse hearts derived from control and obese dams. A Organised myocardium in the control neonatal heart. B Disorganised myocardium in the neonate from obese dam. C. Control lumen in right ventricle D. Hypertrophied right ventricle in obese neonate. (unpublished observations, Henderson et al)
Weights and intakes; Lard Rich Diet; Pregnant Rats

Khan et al, Hypertension 2003
Adult offspring of rat dams fed lard rich diet

Fasting plasma leptin concentration in 9 month old female offspring of fat fed dams (OF, n=10, compared with CON (n=10, * P < 0.05).

Taylor et al, J Physiol 2005
Rats fed ‘junk food’ in pregnancy alone-

13% heavier than controls

Exposure to junk food during gestation and lactation (and greater weight gain) promotes hyperphagia and selective preference for junk foods, as well as weight gain in offspring.

Bayol et al, British J Nutrition 2007
Early maternal undernutrition & refeeding
70% maternal food restriction
30/50% maternal food restriction
50% maternal protein restriction
Severe maternal undernutrition (30% normal diet) induces increased fat mass and reduces offspring locomotor activity.

The ‘couch potato’ rat?

A role for the hypothalamus in programming of appetite and obesity?

*Hypothalamus controls satiety*

Growth trajectory of neurones in satiety centres of developing fetus may permanently affected by leptin, glucose or insulin concentrations to permanently change appetite (Buret et al, 2004; Plagemann et al, 2002)

Is maternal obesity permanently programming the child’s hypothalamic appetite centres?
Animal studies

Suggest increased maternal weight gain detrimental to offspring health

*But*- this has not been primary hypothesis

Low maternal weight gain data unequivocal in showing harm.