Obesity – the imperative for prevention in childhood

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June 20th 2013
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Obesity: like no previous epidemic

- Diabetes
- Cancer
- Dementia
- Cardiovascular Disease
- Asthma
- Arthritis
- All non-communicable diseases

Causes 4000 – 6000 Deaths per year in Ireland (Pop 5 million)

Suicide deaths 486 (2011), Road deaths 161 (2012)
World Economic Forum 2011

- 2009 World Health Spend was $5 trillion ($4.4 trillion spent in high income countries).

- Cumulative loss of output from NCD 2010 to 2030 will be $47trillion (70% World GDP 2010)

- Currently high income countries bear most cost but this will change to middle income/developing areas
Percentage increase in BMI categories since 1986

Sturm and Hattori, Int J Obes 2012
Normal weight finishes at

- BMI: 25 kg/M²
- Male: 12st 4lbs, 78Kgs
- Female: 10st 3lbs, 65 kgs
3 Grades of Obesity

- Overweight: BMI 25-30
- Grade 1: BMI 30-35
- Grade 2: BMI 35-40
- Grade 3: BMI >40

USA: 5% have BMI > 40
Europe: 2% have BMI > 40
Outcomes for Service in SVUH/SCH

- Lost Weight (> 2%) 63%
- Weight Stable (+ or - 2%) 28%
- Gained Weight (> 2%) 9%
Childhood Obesity in Ireland (and Europe)

- 25% 3 year olds overweight/obese
- 25% 9 years olds overweight/obese

- low self image, concept and self esteem

Growing up in Ireland 2009
Younger age of onset, bigger final weight  O’Connell et al, Public Health Nutr. 2010

<table>
<thead>
<tr>
<th>$n$ ((Total=438))</th>
<th>Age of onset of overweight (yrs)</th>
<th>Median BMI ((kg/m^2))</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>56</td>
<td>&lt; 5</td>
<td>52.3</td>
<td>38.9 – 78.2</td>
</tr>
<tr>
<td>77</td>
<td>5 – 10</td>
<td>51.2</td>
<td>31.6 – 73.2</td>
</tr>
<tr>
<td>84</td>
<td>11 – 15</td>
<td>48.3</td>
<td>32.4 – 72.6</td>
</tr>
<tr>
<td>60</td>
<td>16 – 20</td>
<td>48.0</td>
<td>30.1 – 70.5</td>
</tr>
<tr>
<td>54</td>
<td>21 – 25</td>
<td>47.8</td>
<td>32.3 – 81.1</td>
</tr>
<tr>
<td>44</td>
<td>26 – 30</td>
<td>43.9</td>
<td>32.1 – 68.9</td>
</tr>
<tr>
<td>27</td>
<td>&gt; 30</td>
<td>42.9</td>
<td>30.6 – 67.3</td>
</tr>
</tbody>
</table>
• Study cohort - 6328 subjects (2961 male)
  – mean age 11.4 ± 4.0 years at baseline
  – mean length of follow-up 23.1 ± 3.3 years

• 5554 subjects *normal weight as children*
  – 812 (15%) were obese as adults

• 774 subjects *overweight or obese as children*
  – 500 (65%) were obese as adults

• 147 subjects *obese as children*
  – 121 (82%) were obese as adults

*Juonala et al, NEJM 2011*
Outline of talk

• Definition and scale of problem

• What we are learning about obesity
  Causes, effects and research

• Why all roads lead to the imperative of prevention
The determinants of obesity are complex
Sports Drinks

• Growing Up Today Study II
• Large Prospective Study
• 5995 girls/4906 boys
• 9-16 years old
• Consumption of sports drinks strongly associated with weight gain

(Field et al, Consumption of Sports Drinks Prospectively Associated with Greater Weight Gain among Adolescents, Obesity Society Meeting 2012)
Consumption of free sugar has soared
Consumption of sweet beverages and type 2 diabetes incidence in European adults: results from EPIC-InterAct. *Diabetologia*. 2013 Apr 26th

“This study corroborates the evidence between incidence of type 2 diabetes and high consumption of sugar sweetened drinks”
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“This study corroborates the evidence between incidence of type 2 diabetes and high consumption of sugar sweetened drinks”

GSK decision to sell Ribena and Lucozade.
Calories running round the pitch should be illegal

- Lucozade Sport 140 Calories
- Lucozade Energy 350 Calories
- Powerade 80 Calories
- Hydrate BPM 317 Calories
- Mace Glucose Drink 332 Calories
Secondary School Travel 1986-2006

Source: CSO (2009)
5 times more girls drive themselves to secondary school than cycle

- Driving themselves (2,463)
- Cycling (521)
Need environment conducive to exercise
Obesity causes and worsens outcome in......

• Diabetes
• Cancer
• Dementia
• Sleep Apnoea
• Asthma
• Osteoarthritis
• Fatty liver disease
• Psoriasis
• Cardiovascular Disease
• Death from H1N1 (Swine Flu)
Focus our work on the immune system in obesity
Natural Killer Cell

- Key cell in attacking viruses and cancer cells
- Involved in a range of autoimmune conditions
Decrease in circulating natural killer cells in obesity

Natural Killer Cells in Obesity: Impaired Function and Increased Susceptibility to the Effects of Cigarette Smoke

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Moved on to the iNKT cell

A key cell in the innate immune system

Represents 0.2% - 1.2% of circulating T cells

Interacts with other immune cells to determine the downstream immune response:
  - Pro-inflammatory
  - Anti-inflammatory
  - Cytotoxic

- Cytokine
- NK cells
- DCs
- B cells
- Macrophages
- Chemokines
- T cells
- Cytotoxicity
iNKT cells are reduced in human obesity
Could this immune deficiency explain the many complications of obesity?

- Carried out detailed mouse studies in University of Harvard Boston
Immune deficient mice get much fatter

**Fat pads**

WT

Ja18KO

**Weight (g)**

Fat pads

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**Lean mass (g)**

**Fat Mass (g)**

**% Fat**

WT on HFD

Ja18KO on HFD

Lean Mass: 12.3g

Fat Mass: 8.9g

% Fat: 42%

Lean Mass: 12.3g

Fat Mass: 20g

% Fat: 61.9%
**Immune deficient mice have diabetes**

AUC, p=0.002
2 way ANOVA, p=0.002
What happens if you give back iNKT cells?

- Adoptive transfer of iNKT cells

  - Involves intraperitoneal administration of iNKT cells to iNKT cell KO mouse

  - Controls are PBS or T cell preparation excluding iNKT cells

  obese Ja18KO mouse

continue on HFD for 4 days
The mice lose weight and diabetes improves rapidly.
Conclusion

• Weight regulates the immune system

• Immune system regulates weight and glucose
Moved focus to children
## Childrens Baseline Data

<table>
<thead>
<tr>
<th></th>
<th>Lean</th>
<th>Obese</th>
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<tbody>
<tr>
<td>Age</td>
<td>12.6 yrs old</td>
<td>11.9 yrs old</td>
</tr>
<tr>
<td>Number</td>
<td>20</td>
<td>30</td>
</tr>
<tr>
<td>Weight</td>
<td>52kgs</td>
<td>90kgs</td>
</tr>
<tr>
<td>Glucose</td>
<td>4.9</td>
<td>5.1</td>
</tr>
<tr>
<td>Insulin</td>
<td>21</td>
<td>149</td>
</tr>
</tbody>
</table>
Reduction in iNKT cells number and function already present in obese children.
Gene expression for diabetes and heart disease

miR-33a/b contribute to the regulation of fatty acid metabolism and insulin signaling

Gene expression for Cancer defence

miR 34a – Tumour Suppressor

Incidence of New Cancers Worldwide Will DOUBLE Between 2002 and 2030

Source: US Center for Disease Control
Summary in Children

• Innate immune system is switching off

• Genes for type 2 diabetes and heart disease are switched on

• Genes for stopping cancer are switched off
The Imperatives for prevention

• Health Burden

• Financial Cost

• There is no way back
Lancet February 2013

Profits and pandemics: prevention of harmful effects of tobacco, alcohol, and ultra-processed food and drink industries

Rob Moodie et al on behalf of The Lancet Non Comunicable Disease Action Group