The Science of Obesity & Increased Disease Risk in Children: Implications for Intervention Strategies

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Prevalence Rate of BMI >85th Percentile (National Longitudinal Study of Youth)

<table>
<thead>
<tr>
<th>Year</th>
<th>Caucasian</th>
<th>African American</th>
<th>Hispanic</th>
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Strauss et al; JAMA 2001

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Recent increase in prevalence of obesity is probably due to the Interaction between a normal physiology and an obesity promoting environment (greater abundance of food, less requirement for physical activity).

An evolutionary adaptation - storage of energy required for survival

Negative health outcome in susceptible individuals
This Reversal of Fortune has also affected Children

- Recess, PE Play
- Cramming at school
  - Focus on scores
  - Lack of safe play; more TV
- Healthy home cooking
- Vending machines
  - Convenience lunches

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The Average Adult Turns Over 1 Million Calories per Year

2% error leads to obesity

~50 kcal/day, or, 20 min of walk instead of TV
$3.99
1,250 calories
Obesity not simply due to overeating or inactivity

But,

A breakdown in the homeostatic regulation to balance energy in to energy out
Major Obesity Related Diseases & Health Impact

- Cardiovascular disease
- Type 2 diabetes
- Stroke
- Cancer
- Asthma
- Gallbladder disease
- Psychosocial issues
- Eating disorders

- 300,000 deaths/year (second to tobacco)
- $100 billion/year
- $15 billion in CA
Theories Linking Body Fat to Health Outcomes?

- Portal theory
- Ectopic fat
- Fat as an endocrine organ
Cross-sectional CT image of Adipose Tissue in the abdomen

- Subcutaneous
- Intra-abdominal or visceral

- Measured by imaging
- More metabolically active
- Protects organs
- Drains to hepatic portal vein
Diabetes and Gestational Diabetes Trends Among Adults in the U.S., BRFSS 1990, 1995 and 2001

Stats on Type 2 Diabetes in Children & Adolescents

- Major risk factors are overweight, family history and being African American, Hispanic or Native American
- 20-fold increase in the incidence of T2D in youth in last 20 years
- 1 in 3 overweight minority children have pre-diabetes
- Most overweight children also have other elevated risk factors (high blood pressure, high cholesterol)
- Not a new problem: studies from 30 years ago found T2D in obese children
Type 2 Diabetes in Children:

Hispanic boy at LA County hospital who volunteered for a research study

- 352 pounds
- Total cholesterol = 200
- Triglyceride level = 151
- Fasting glucose = 129
- 2-hour glucose = 250
- Referred for treatment

There is no major screening/educational program for high-risk children in LA county hospital
Insulin resistance
Failure to compensate
Type 2 Diabetes/Hyperglycemia

Puberty (transient)

Ethnicity

Genetic factors

Obesity/Visceral Fat/“Ectopic” Fat

Appropriate Compensation

Dyslipidemia
High BP

Atherosclerosis
Hypertension

Normal glucose
High insulin

FFA↑

Unhealthy B-cell

Failure to compensate

Physical Inactivity/Diet factors

Health

FFA↑

Healthy B-cell

Appropriate Compensation

Obesity/Visceral Fat/“Ectopic” Fat

Puberty (transient)

Ethnicity

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Obesity/Visceral Fat/“Ectopic” Fat

Appropriate Compensation

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Normal glucose
High insulin

FFA↑
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Range of Insulin Resistance in Children

- Insulin Sensitivity of Tissues
- Insulin Secretion by Pancreas

- Healthy Weight
- Pre-pubertal
- Pubertal
- Overweight
- Extreme Overweight
- Hispanic or African American

- Weight loss
- TZDs - beta cell rest
- Diet - CHOs
- Resistance training
Comparison of 3 ethnic groups in Los Angeles

<table>
<thead>
<tr>
<th></th>
<th>Caucasian (n=12)</th>
<th>Af Am (n=13)</th>
<th>Hisp (n=32)</th>
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<tr>
<td>Age (y)</td>
<td>10.9 ± 1.9</td>
<td>10.6 ± 1.7</td>
<td>10.2 ± 2.0</td>
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<tr>
<td>Weight (kg)</td>
<td>45.0 ± 17.2</td>
<td>51.5 ± 16.7</td>
<td>48.3 ± 16.5</td>
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<tr>
<td>Fat Mass (kg)</td>
<td>13.0 ± 8.1</td>
<td>15.4 ± 8.7</td>
<td>15.7 ± 8.9</td>
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<tr>
<td>% Fat</td>
<td>26.5 ± 9.4</td>
<td>27.9 ± 10.0</td>
<td>30.8 ± 9.2</td>
</tr>
<tr>
<td>Lean Mass (kg)</td>
<td>30.0 ± 9.1</td>
<td>33.8 ± 8.8</td>
<td>30.5 ± 8.7</td>
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</tbody>
</table>
Compensatory response to insulin resistance is ethnic specific:

- AA reduce insulin clearance
- Hispanics increase secretion

Goran et al; Diabetes Care 2002
Prevalence of IGT: No Effect of Obesity Status

Goran et al; JCEM 2004
Higher Prevalence of IGT in Children Exposed to GDM

Goran et al; JCEM 2004
**B-cell Compensation in Obese Hispanic Children with a Positive Family History**

Increased risk due to requirement for sustained compensatory increase in insulin secretion? “the pancreatic exhaustion theory”

Increased risk since already compensating poorly? “the pancreatic inability to compensate theory”

Goran et al; JCEM 2004
Metabolic Syndrome in Overweight Hispanic Youth

- Clustering of metabolic risk factors
  - High blood pressure
  - High central fat
  - High glucose
  - Low HDL
  - High triglyceride
- Defined as 3 or more of these features
- 25% of Hispanic adults have MS
% of Children With Features of the Metabolic Syndrome in Overweight Hispanic Children

Feature
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Cruz et al; JCEM 2004
% of Children With Features of the Metabolic Syndrome in Overweight Hispanic Children

Number of Features

Cruz et al; JCEM 2004

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Insulin Sensitivity According to Number of Features of the Metabolic Syndrome

Data adjusted for gender, age, total body fat and total lean mass;
Also SI was significantly and independently related to HDL, TG and sysBP

Cruz et al; JCEM 2004

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Implications for Treatment/Prevention
The Good News:
Childhood Obesity and Type 2 Diabetes Can be Prevented

- Breastfeeding
- Reduced TV; promotion of physical activity
- Teach healthy eating early
- Healthy food and access to play and PE in schools
- Family based approaches
- Screening is important to monitor the “silent epidemic”
- In adults, lifestyle intervention and/or pharmacological intervention can prevent onset of diabetes in high risk
What Should Interventions be Trying to Modify?

- Most prior interventions have targeted body weight/BMI
  - May take generations to reverse the population BMI trend
  - Weight loss may be effective but not usually sustainable
  - Weight loss per se does not necessarily address health risk
  - Not all overweight individuals have elevated risk factors
Dieting in Children Leads to Greater Weight Gain

- Cohort study in 6,769 children and adolescents
- Infrequent dieting in 25% girls and 14% boys
- Frequent dieting in 5% girls and 2% of boys
- Frequency of dieting was associated with greater weight gain over a 3-year period

Field et al, 2004
What Should Interventions be Trying to Modify?

- Interventions designed to target specific metabolic factors/health outcomes may be more effective esp in high risk groups
  - Addressing features of the MS may be an efficient approach since multiple risk factors are targeted through one common mechanism
  - Eg does improvement in insulin resistance improve risk of T2D and CVD risk?
Pharmacological Approaches?

- Obesity drugs effective in children but no long term data on effect and safety
- Metformin - - improves BMI and reduce insulin; no effect on insulin sensitivity
- TZD’s – been used to prevent type 2 diabetes in Hispanic women with GDM.
  - May provide temporary relief to b-cell by improving insulin sensitivity and temporarily reducing secretory demands. May be useful in extreme situations
- Interaction with puberty?
- Different approaches for different populations.
Popular Diet Approaches:

- All provide quick fixes and don’t help sustain weight loss;
- Usually get initial weight loss b/c all approaches limit calories in some way
- Focus is on calories and weight rather than health risks
- Most target white middle class individuals
- Need more diet/activity approaches for high-risk sub-groups
- Needs to be flexible & individualized!
Nutrition Approaches in Children and Adolescents

- Remarkably understudied.....
- A few large scale school based studies
  - Positive changes in schools (eg increase fruit and veg; reduced fat)
  - Little effect on BMI or other metabolic outcomes
  - Tough to extend effects beyond the school

- Other approaches needed
  - Types of fat (replace sat fat and trans fat with plant based sources and PUFA eg soy), water, fiber, plant sterols, omega-3-fatty acids, whole grain, lower GI etc
  - Need smaller scale “proof of concept” studies
  - Need social marketing of healthy food - make healthy food more glamorous to kids
  - Dietary interventions may need to address specific minority health issues (eg higher BP in AA, higher TGs in Hispanics)
Macronutrients, weight control & health

- Data suggest that type of fats and carbohydrates are more important than the amount.
- For fat: replace foods high in saturated fat and trans fatty with foods rich in plant based sources (MUFAs and PUFAs; nuts, fish, soy).
- For CHO: replace foods based on simple/unprocessed CHO with foods high in whole grain/processed CHO, fiber and low glycemic index value.
Glycemic Index

- Low GI means a smaller rise in blood glucose levels after meals and can improve insulin sensitivity
- Low GI diets can help with weight loss as feel fuller for longer
- In a trial in children, low GI foods at breakfast significantly reduced food intake at lunch by about 100 kcal (Warren; Pediatrics 2003)
Reduced Glycemic Load Diet in Treatment of Adolescent Obesity

- Randomized pilot trial in 14 obese adolescents
- Intervention emphasis on reduced GL diet versus a conventional (reduced fat) diet
- Outcomes at 6 and 12 months suggest reduced BMI, body fat and improved insulin resistance

Ebbeling et al, 2003
Lifestyle Intervention Improves Insulin Levels in Native American Youth

- School based intervention over 3 years
- Intervention included education and environmental components aimed at reducing sugared beverages
- Provided water coolers and replaced sodas in vending machines
- By 3 years fasting and 30-minute plasma insulin had reduced among NA youth to levels found in Caucasians

Ritenbaugh et al, 2003
# Individualized Dietary Modification:

14 year old Overweight Hispanic Girl

**Breakfast**
- Low fat fruit yogurt
- Chocolate glazed doughnut
- Fresh corn tamale with milk
- Gatorade (6 fl oz)

**Lunch**
- Capri juice cooler (6 fl oz)
- Fruit rollup
- Cupcake with chocolate frosting
- Lollipop

**Dinner**
- Beef top sirloin
- Spanish rice
- Pepsi (12 fl oz)
- Chewing gum
- Chocolate candy
- Cherry juice drink (6 fl oz)
- Tamarind fruit (1 cup)

## Summary of Diet Profile Before
- 2204 Kcal
- 70% calories as CHO
- 21% calories as fat
- 83 g protein
- 4.0g fiber per 1000 kcal
- 33% calories from sugar

## Summary of Diet Profile After
- 2145 Kcal
- 52% calories as CHO
- 34% calories as fat
- 15.0g fiber per 1000 kcal
- 10.5% calories from sugar

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## Atkins/low CHO?

- Custom-fit healthy exchange

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Role of Physical Activity in Improving Insulin Sensitivity

- Decline in physical activity in children may have contributed to state of greater insulin resistance during growth and development
- Physical activity interventions in adults improve glucose metabolism
- Extremely limited information in children
- Type of activity (aerobic vs strength may be critical to address risk factors beyond BMI)
- Response to different forms of exercise intervention may be different across ethnic groups
Resistance Training in Youth

- Safe and effective at improving strength
- Overweight kids can excel
- Limited studies on other outcomes.
- In a study of overweight Caucasian girls (n=12; 3d/wk for 20 wks)
  - increased strength
  - reduced visceral fat accumulation.
  - Small (but non-significant) improvements in glucose tolerance

![Graph showing glucose levels before and after exercise.](image-url)
Effects of 16 wk of Resistance Training in Overweight Boys

- Training
- Control

Graph showing changes in insulin sensitivity before (Pre) and after (Post) 16 weeks of resistance training.
Media and Childhood Obesity:
Kaiser Family Foundation Report, 2004

- X-sectional and intervention studies support the evidence that increased TV/media is associated with obesity
- The nature of TV viewing (how and what) may be as important as how much
- Children see 40,000 TV ads/year
  - double that of 1970
  - 11 food commercials per hour on Saturday mornings
  - primarily for candy (32%), cereal (31%) and fast food (9%)
  - 17% of commercials offer a free toy
  - Children who watch more TV tend to choose less healthy choices in a controlled trial
- A role for media policy to prevent and reduce childhood obesity
Reduced TV Intervention: Controlled Trial

- Randomized pilot trial in 2 schools (192 3rd/4th grade children)
- 18 lesson, 6 month intervention designed to reduce TV/media

Robinson et al, 1999
Interactive Multimedia for Promoting ACTivity in children (IMPACT): Edutainment

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and Kim Reynolds, PhD

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The Cultural Evolution of Coffee

A cup of coffee

Tall
Grande
Venti

Short
Some Recent Developments

- Kraft Global Initiative (July 2003)
  - Cap on portion sizes of single serve packages
  - Better nutritional guidelines for products
  - Gradual & meaningful improvements in product line
  - Elimination of in-school marketing
  - Guidelines for advertising and media

- McDonalds “Eat Smart, be Active” and downsizing (March 2004)
  - Phase out supersize drinks & fries (from 7oz to 6oz)
  - Bagels optional at breakfast
  - Switch from 2% to 1% milk
The Next Food Evolution?

HAPPY MEALS ➔ HAPPY HEALTHY MEALS
Summary & Conclusion

- Obesity is increasing in all ages esp in high risk sub-groups
- BMI is the common tool for “tracking” obesity but has problems (does not reflect fat or actual disease risk factors)
- Obesity is likely an evolutionary adaptation to overabundance of food and sedentary life-style (the “obesogenic environment”)
- Obesity occurs when there is a mismatch in regulation of energy balance
- Obesity only becomes a health issue is some
  - Unknown predisposing factors, eg poor beta-cell control
  - May depend on where fat is stored and metabolic/endocrine effects of fat cells
- Impact of fat on health is worse in some groups (eg blacks and hispanics)
  - There are distinct ethnic differences in compensatory response to insulin resistance
- The pathogenesis linking fat to disease is evident early in life and may even be affected by in utero factors
Summary Continued

- Overweight Hispanic children at extreme high risk for both type 2 diabetes and cardiovascular disease
  - Highlights need for screening and prevention
- Obesity and its related conditions can be prevented but need much better individualized, “custom-fit” interventions that are effective and long-lasting and address underlying physiology
- Insulin resistance may be a good intervention target since it addresses multiple risks and probable common pathway
- Need more collaboration between research and food industry
- Need more social marketing of healthy foods for children

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