Preventing Obesity and Type 2 Diabetes in Youth

Phil Zeitler MD, PhD
University of Colorado Denver
Obesity Among U.S. Adults 2009
The Prevalence of Childhood Obesity Continues to rise in US

NHANES/CDC Report
Year of presentation

% new onset patients with T2DM

New Onset T2D in Youth (0-19)

A worldwide phenomenon

Pinhas-Hamiel and Zeitler J Pediatr. 146:693-700, 2005
Who are these kids?

Is this environment?

Are they a genetic “extreme”?

If so, why now?
Unique aspects of type 2 in youth
Current US Demographics

• 1211 kids screened for a large study of T2D
  – Average age 14.2
  – 37% male
  – Average BMI 35
  – Ethnicity
    • 21% white
    • 34% Hispanic
    • 35% African-American
    • 5% American-Indian
    • 2% Asian
Current Incidence of T2D in Adolescents

- SEARCH for Diabetes in Youth
  - rare in children younger than 10 years of age, regardless of race or ethnicity.
  - after 10 years of age, newly diagnosed cases
    - 14.9% in non-Hispanic whites (NHW)
      - 0.19 cases per 1000 NHW youth
    - 46.1% in Hispanic youth
    - 57.8% in non-Hispanic Blacks (NHB)
    - 69.7% in Asian/Pacific Islanders
    - 86.2% in American Indian (AI)
      - 1.74 cases per 1000 AI youth
  - In total, approximately **3700** youth under 20 years of age are diagnosed with T2D in the US annually

The prevalence of undiagnosed diabetes is low

- **NHANES 1999-2000** – 915 12-19 years
  - DM based on fasting criteria < 1%

- **STOPP-T2D**
  - 1750 8th graders, BMI > 85%ile
    - 0.4% - DM – fasting criteria
    - 0.1% - DM - OGGT
    - 2% with IGT

Williams et al Pediatrics 116: 1122-1126, 2005
Baranowski et al Diab Care 29:212-217
The Prevalence of Impaired Fasting Glucose is high

• NHANES 1999-2000 – 915 12-19 years
  – All adolescents IFG 7%,
    • 13% Mexican-Americans
    • 7% African-Americans
    • 4% NHW
  – Obese Adolescents 11.7%

• STOPP-T2D
  – 1750 8th graders, BMI > 85%ile
    • 40.5% IFG
    • 2% IGT

Williams et al Pediatrics 116: 1122-1126, 2005
Baranowski et al Diab Care 29:212-217
The Type 2 Family

- 45% of mothers and 40% of fathers with T2D
- 27% both parents with T2D
  - 50% of the remaining fathers diagnosed with T2DM in the study
  - Parents have poor DM control
    - mothers A1c: 13.4 ± 1.6 %
    - Mothers, fathers AND siblings obese

The Type 2 Family

- Diet high in fat, low in fiber
  - Doesn’t make a difference if mother has T2D
- Binge Eating prevalent
- No routine activity
- 3-5 hours/day TV
- Insulin resistance prevalent among unaffected family members

The Type 2 Family – newer insights

- Frequent family dysfunction
  - Unstable residence and transportation
  - Contact with justice system
  - School absences or dropouts
  - Poor communication
  - Poor parenting
  - Domestic violence

- Increased family health burden
  - Diabetes and non-diabetes related disorders
  - Psychological and psychiatric disorders in parents and family members.
## Psychosocial Characteristics

<table>
<thead>
<tr>
<th>Lives with **</th>
<th>Non-Hispanic White</th>
<th>Hispanic</th>
<th>Non-Hispanic Black</th>
<th>American Indian</th>
</tr>
</thead>
<tbody>
<tr>
<td>Both parents</td>
<td>43%</td>
<td>43.2%</td>
<td>26.8%</td>
<td>46.5%</td>
</tr>
<tr>
<td>Mother only</td>
<td>40%</td>
<td>46.3%</td>
<td>58.2%</td>
<td>25.6%</td>
</tr>
<tr>
<td>Father only</td>
<td>11.1%</td>
<td>3.2%</td>
<td>3.8%</td>
<td>7.0%</td>
</tr>
<tr>
<td>Neither</td>
<td>5.9%</td>
<td>7.4%</td>
<td>11.3%</td>
<td>20.9%</td>
</tr>
</tbody>
</table>

** P < 0.01

The Today Study Group
J Clin Endocrinol Metab *in press*
### Psychosocial Characteristics

<table>
<thead>
<tr>
<th>Lives with **</th>
<th>Non-Hispanic White</th>
<th>Hispanic</th>
<th>Non-Hispanic Black</th>
<th>American Indian</th>
</tr>
</thead>
<tbody>
<tr>
<td>Both parents</td>
<td>43%</td>
<td>43.2%</td>
<td>26.8%</td>
<td>46.5%</td>
</tr>
<tr>
<td>Mother only</td>
<td>40%</td>
<td>46.3%</td>
<td>58.2%</td>
<td>25.6%</td>
</tr>
<tr>
<td>Father only</td>
<td><strong>11.1%</strong></td>
<td>3.2%</td>
<td>3.8%</td>
<td>7.0%</td>
</tr>
<tr>
<td>Neither</td>
<td>5.9%</td>
<td>7.4%</td>
<td>11.3%</td>
<td>20.9%</td>
</tr>
</tbody>
</table>

** P < 0.01

The Today Study Group
J Clin Endocrinol Metab *in press*
Parental Education Attainment

**

The Today Study Group
J Clin Endocrinol Metab in press
102 obese children and adolescents

NGT
N=71

NGT
N=65 (91.5%)

IGT
N=6 (8.5%)

NGT
N=10 (32.3%)

IGT
N=11 (35.4%)

T2DM
N=10 (32.3%)

Mean follow-up of 21 months

Weiss R. et al Diabetes Care, 2005
Factors Associated With The Transition Between Categories of Glucose Tolerance

- Marked weight gain
- Profound insulin resistance at baseline
- Reduced first phase insulin secretion at baseline

Weiss R. et al Diabetes Care, 2005
Insulin resistance and puberty

Moran et al J Clin Endocrinol Metab 87:4817-4820, 2002
Pima Indian Sib Pairs Discordant for Diabetes and Exposure to Diabetes in Utero

Number of sib pairs

Born Before or After Mother's Diagnosis

Born Before or After Father's Diagnosis

OR = 3.0, p<0.01

OR = 1.3, ns.

Dabelea et al, Diabetes, 49, 2000
Preventing type 2 diabetes in youth

• Preventing development of insulin resistance
  – Prevention of visceral adiposity
  – Preventing worsening of the routine insulin resistance of puberty
• Preventing maternal obesity, weight gain, and gestational diabetes
• Accomplishing this in a setting of disrupted family structure and low socioeconomic status.
Energy Balance
A obesity culture for kids

- **dietary changes**
  - fast food
  - snacking
  - high caloric density
  - cheap
  - increased portion size

- **Cultural changes**
  - never hungry
  - Advertising assault
  - energy saving
  - automobiles vs. pedestrians

- **activity changes**
  - decreased active time
  - decreased school PE time
  - decreased play time at home
  - expenses associated with sports
  - emphasis on excellence
  - lack of supervision

- **increased sedentary time**
  - computers
  - video games
  - 64 channel TV
  - lack of supervision
Energy Balance: Television

• Average # hrs/day a TV is on in an American household:
  – 6 hours, 45 minutes (405 minutes)
• Typical time spent in aerobic activity
  – 8 - 10 minutes
• 66% of Americans watch TV during dinner
• Hours/year in school: 900
• Hours/year watching TV: 1500
• Fast food is the #1 TV advertisement aimed at kids
• 4 hrs of Sat a.m. cartoons = 200 “junk food” ads

Statistics provided by TV-Free America
Energy Balance: Nutrition

- Consumption of sugar beverages
- Americans eat approximately 1/3 meals outside home
- Most of these meals are high fat, low nutrient
- High fat food intake leads to more high fat food intake
- Family eating practices are key
  - What are the parental eating practices?
  - Are meals eaten together?
  - Is there a “dinner table”?

Jelalian, 2007; Trost et al., 2001; Fitzgibbon & Stolley, 2004)
Trips to School by Distance and Mode
Youth Aged 5–15 Years

One Mile or Less

- Auto: 51
- School Bus: 14
- Walk: 31
- Bike: 3
- Other: 1

More than One and Less than or Equal to Two Miles

- Auto: 50
- School Bus: 41
- Walk: 5
- Bike: 1
- Other: 3
Behavior and Energy Balance

• **INTAKE**
  • Burger King Meal
    - Triple Whopper w/Cheese
      • 1230 calories/82g fat
    - Large Fries
      • 600 calories/33g fat
    - Large Milkshake
      • 1236 calories/36g fat
  • **TOTAL**
    - 3066 calories/233g fat

• **EXPENDITURE**
  • Burning 3066 calories
    - Run 30 miles
Lifestyle Modification
In principle, it’s easy!

• Reduce the accretion of visceral fat through lifestyle modification
• Reverse the trends in the toxic environment through thermodynamics
  – Reduce caloric intake
  – Increase caloric expenditure
Lifestyle Modification

• AAP Expert Committee:
  – Evidence based dietary interventions
    • Eliminate liquid calories
    • Reduce or eliminate eating out
    • Reduce portion sizes
  – Evidence based activity interventions
    • Reduce sedentary time/screen time
    • Encourage attainment of recommended activity goals.

Barlow et al Pediatrics 120:S164-192, 2007
In practice, it’s difficult!

• Individual medical
  – Limited evidence for effectiveness
  – Labor intensive and low yield
• Home-based intervention
  – Limited research
• School-based intervention
• Change in the social and built environment
Individual interventions

- Diet change is key to successful weight loss
- Exercise required to maintain loss
- Increasing daily activity better than “formal” exercise
- Parents are critical
  - Parental obesity is a predictive factor
  - Parent/child >> Child alone
  - Parent >> child
- Caveat: all studies done on families presenting for weight loss!
  - Relevance to children referred for health problems?
Cochrane Meta-analyses

• Summerbell 2007 – **No** evidence for effectiveness of school-based interventions for the prevention of obesity
  – Some evidence for reported changes in dietary habits

• Summerbell 2007 – **No** evidence for effectiveness of school-based interventions for the treatment of obesity
Medications?

- Diabetes Prevention Program
  - Lifestyle intervention and metformin, effective in reducing progression of IGT to T2DM in adults
    - Lifestyle more effective in older participants
    - Metformin equally effective in younger participants
  - No youth involved
  - All participants had IGT
  - What is the evidence that metformin is useful in youth
Metformin

• Non-controlled case studies
• Freemark and Bursey
  – 29 mixed white and black boys and girls
  – BMI > 30 kg/m2, Fasting insulin > 15
  – At least 1 1st or 2nd degree relative with T2DM
  – Metformin 500 mg BID or placebo for 6 months
  – BMI decreased 0.12 SD (1%) vs. increase of 0.23 SD (2%)
  – Decreased fasting glucose (all normal) and insulin

Freemark and Bursey, Pediatrics 107: E55, 2001
Metformin

– Love-Osborne et al.
  • 58 kids 12-19
    – BMI > 95%ile
    – Fasting insulin > 15 or HOMA > 2.5
  • Randomized to metformin or placebo for 6 months
  • No difference in weight loss between groups overall
  • No significant change in glucose, insulin, lipids, HOMA

DPP for Youth?

- Progression to diabetes is ~7% in 8 years with NGT among insulin-resistant Hispanic adolescents.
- Assume metformin reduces progression by the same order of magnitude as in IGT adults (~0.3% progression vs ~0.5% every 6 months).
- Assume 5% dropout every 6 months.
- Study would need 5000 kids and last 6 years to get 80% power to see the difference.
Summary

• Insulin resistance is the underlying defect in risk for type 2 diabetes
• The development of Type 2 diabetes reflects the progressive loss of compensation for insulin resistance due to $\beta$-cell failure
• Fat depots play an important role in insulin resistance and $\beta$-cell failure
• Prevention of type 2 diabetes in youth will require reversal of fat accumulation through reduction in caloric intake and increase in caloric expenditure
• We do not yet know how to accomplish this given the complex social and cultural factors involved
Thank you for your attention

The Big Texan – Amarillo, Texas