DIETARY SUGARS AND RISK FACTORS FOR CARDIOVASCULAR DISEASE IN CHILDHOOD

Rae-Ellen W. Kavey, MD, MPH
University of Rochester Medical Center
I have no potential conflicts of interest to disclose.
OVERVIEW

• Development of taste preferences
• Current dietary intake of added sugars in children and adolescents
• CV risk factors associated with high added sugar intake
• Clinical interventions addressing high added sugar intake
DEVELOPMENT OF FOOD PREFERENCES

• There is an innate preference for sweetness with newborns responding positively and preferentially to a sweet taste
  (Bartoshuk LM. Annu Rev Psychol 1994;45:419-440)

• High sucrose concentrations have been shown to have an analgesic effect in neonates
TOTAL CRYING TIME AFTER HEEL STICK WITH WATER, 12.5%, 25% & 50% SUCROSE

Haouari B et al
BMJ 1995;310:1498-1502
Children’s Medical Ventures’ Sweet-Ease® helps to calm and soothe babies up to six months old. Carefully preformulated in aseptically packaged cups, the 24% sucrose solution can be used anywhere in the hospital or in a pediatrician’s office to help distressed babies. With no artificial ingredients or preservatives, Sweet-Ease® is the pure and simple sucrose solution.
DEVELOPMENT OF FOOD PREFERENCES

- Studies in monozygotic and dizygotic twins show evidence for hereditability in food preferences
  (Breen FM et al. Physiol Behav 2006;88:443-7)

- Prenatal and early postnatal exposures to a flavor in amniotic fluid and/or breast milk enhance an infant’s enjoyment of that flavor when introduced later as a solid food
DEVELOPMENT OF FOOD PREFERENCES

- Parents powerfully shape children’s early experiences with food:
  - Determine selection and availability
  - Model eating behavior
  - Feeding style including use of food as reward
Children’s food preferences: A longitudinal analysis

- 70 child/mother pairs followed X 6 yrs
- Mothers completed food preference questionnaire for child at 2-3 yrs of age(T1), at 4 yrs(T2) and 8 yrs(T3); and for themselves at T1 and T3.
- Strongest predictors of foods liked by children at T3 were those liked by mothers at T1 & T3
- In MVA, mothers’ and children’s food preferences were significantly correlated
FAMILIAL AND ENVIRONMENTAL IMPACT ON DIET PREFERENCES

• Repeated exposure promotes acceptance of initially disliked foods
• Environmental exposures including child-oriented commercials significantly influence food choices
Between 5 and 14 exposures to a new food are needed to develop acceptance.

TRACKING OF FOOD PREFERENCES:

Girls’ early sweetened carbonated beverage intake predicts different patterns of beverage and nutrient intake across childhood and adolescence


- Longitudinal study of non-Hispanic white girls & their parents assessed biennially from age 5 to 15 years using 24-hour diet recall
- Girls were categorized as either soda consumers or non-consumers at age 5 yrs
- Soda consumers had higher subsequent soda intake, lower milk intake, higher intake of added sugars & lower intakes of protein, fiber, vit D, calcium, magnesium, phosphorus and potassium from 5 to 15 yrs
Diet preferences are acquired early in childhood and persist into adult life.

Infant feeding practices and early flavor experiences in Mexican infants: An intra-cultural study

“Food practices form the core of a culture’s most cherished beliefs and are passed from one generation to the next”
ADDED SUGAR SOURCES IN CHILDREN’S DIETS
# Added Sugar Sources in Children’s Diets


<table>
<thead>
<tr>
<th>Food Category</th>
<th>2-5 y (%)</th>
<th>6-11 y (%)</th>
<th>12-17 y (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sugars/sweets</td>
<td>20.9%</td>
<td>20.8%</td>
<td>~ 16%</td>
</tr>
<tr>
<td>Regular soda</td>
<td>14.6%</td>
<td>21.9%</td>
<td>~ 39%</td>
</tr>
<tr>
<td>Fruit drinks</td>
<td>19.4%</td>
<td>13.4%</td>
<td>~11%</td>
</tr>
<tr>
<td>Fruit juice</td>
<td>2.3%</td>
<td>1.7%</td>
<td>~1%</td>
</tr>
<tr>
<td>Grains (cereal,etc)</td>
<td>28.2%</td>
<td>27.1%</td>
<td>~17%</td>
</tr>
<tr>
<td>Milk/ Dairy products</td>
<td>10.3%</td>
<td>10.6%</td>
<td>~7%</td>
</tr>
</tbody>
</table>
SUGAR CONTENT OF REGULAR SODA
SPORTS BEVERAGES: THE NEW SSB

- Consumption of sports beverages by children in non-athletic situations is increasingly common.
- Among adolescents, 56.4% reported having consumed a sports drink in the previous week.

CARDIOVASCULAR RISK FACTORS ASSOCIATED WITH HIGH ADDED SUGAR INTAKE

- Obesity
- High blood pressure
- Dyslipidemia
- Hyperinsulinemia
- Metabolic syndrome cluster

Reviewed by Dr. Daniels
MAJOR LIPID METABOLISM PATHWAYS
HEPATIC METABOLISM OF GLUCOSE AND FRUCTOSE

Fructose

Fructose

Fructokinase

Fructose 1-P

Glyceraldehyde

Fructose 1,6-bisphosphatase

Fructose 6-P

Glucokinase

Glucose

Glucose 6-P

Glycogen

Phosphoglucoisomerase

Insulin

Glucagon

Fructose 1,6-bisphosphate

Phosphofructokinase

ATP

Citrate

Dihydroxyacetone

Glyceraldehyde 3-P

Glycerol 3-P

Pyruvate

Lactate

CO₂ + ATP

Acetyl-CoA

Acyl-CoA

Acyl glycerols

VLDL
HEPATIC METABOLISM OF GLUCOSE AND FRUCTOSE

• Glucose enters the glycolytic pathway and stimulates insulin release, breaks down into glyceraldehyde 3-P (ultimately available as energy) and dihydroxyacetone phosphate (→ glycerol 3-P→ acyl glycerols → VLDL/TG)

• Fructose bypasses the entry point for glycolysis and is converted to either glyceraldehyde or dihydroxyacetone phosphate → glycerol 3-P→ acyl glycerols → VLDL/TG
HEPATIC METABOLISM OF GLUCOSE AND FRUCTOSE
COMBINED DYSLIPIDEMIA IN CHILDHOOD

- Mild elevation in LDL-C, moderate to severe elevation in TG, reduced HDL-C = Combined dys- or hyperlipidemia
- High carbohydrate diet increases TG, by enhancing hepatic synthesis of VLDL → overproduction of TG & apo B
- Inverse association between high VLDL/TG and low HDL
- Multiple phenotypes associated with this pattern but almost always seen with obesity in childhood
- Most common referral pattern in pediatric lipid clinics
- Lipid pattern associated with the metabolic syndrome
COMBINED DYSLIPIDEMIA/ ELEVATED TG AS A RISK FACTOR FOR CV DISEASE

- The Young Finns study has followed more than 3000 children in Finland from early childhood to now 30-40 yrs of age.
- At mean follow-up of 21 yrs, subjects with combined dyslipidemia in childhood had significantly increased cIMT, a measure of subclinical atherosclerosis, even after adjustment for contemporary risk factors.

COMBINED DYSLIPIDEMIA/ ELEVATED TG AS A RISK FACTOR FOR CV DISEASE

- The Princeton study followed up 808 subjects after fasting lipid analysis at a mean age of 12 yrs in 1973-1976. After 22 to 31 yrs, 19 cases had experienced at least one CV event at a mean age of 38.5 yrs.
- Elevated childhood and young adult TG levels were consistently and independently associated with young adult CVD (Hazard ratio: 5.35 [CI:1.69-20.0] per 1 unit increase natural log scale)

(Morrison JA et al. Metabolism Clin Exper 2009;58:1277-1284)
# PREVALENCE OF ABNORMAL LIPID LEVELS BY OBESITY STATUS

<table>
<thead>
<tr>
<th>BMI</th>
<th>High LDL (%(95%CI))</th>
<th>Low HDL (%(95%CI))</th>
<th>High TG (%(95%CI))</th>
<th>≥1 Lipid abnormality (%(95%CI))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>5.8 (4.3-7.8)</td>
<td>4.3 (3.3-5.6)</td>
<td>5.9 (4.6-7.5)</td>
<td>14.2 (12.1-16.6)</td>
</tr>
<tr>
<td>Overweight</td>
<td>8.4 (5.4-12.8)</td>
<td>8.3 (4.8-13.9)</td>
<td>13.8 (9.6-19.5)</td>
<td>22.3 (18.0-27.4)</td>
</tr>
<tr>
<td>Obese</td>
<td>14.2 (10.2-19.6)</td>
<td>20.5 (16.3-25.5)</td>
<td>24.1 (18.8-30.3)</td>
<td>42.9 (36-50.1)</td>
</tr>
</tbody>
</table>
Management of Combined Dyslipidemia/Elevated TG in Childhood

- Weight loss
- Change in diet composition
- (Medication)
Diet Composition: Limiting Sugar/Carbohydrate As Treatment for Obesity +/− Dyslipidemia
LOW CARBOHYDRATE DIET FOR WEIGHT LOSS

• 12 week trial; 30 obese adolescents, 12 – 18 yrs of age, randomized to low fat or low carbohydrate diet
• Low fat (LF): <40 g/d of fat with 5 servings of starch/d + unlimited fat-free dairy, fruits and vegetables. No juice or SSBs.
• Low carbohydrate (LC): <= 20 g of carbohydrate/d; unlimited intake of protein & fat X 2 weeks; weeks 3 – 12, carbohydrate increased to 40 g/d by adding nuts/ fruits/ whole grains
• No limitation of calories in either group
• 30 mins of exercise, 3 X week recommended for both groups

(Sondike SB et al. J Pediatr 2003;142:253-8)
## RESULTS

<table>
<thead>
<tr>
<th>Group</th>
<th>BMI (kg/m²)</th>
<th>TC (mg/dL)</th>
<th>TG (mg/dL)</th>
<th>HDL-C (mg/dL)</th>
<th>LDL-C (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Carb</td>
<td>-2.4 +/-2.7</td>
<td>-3.7 +/-18.0</td>
<td>-48.3 +/-29.0 *</td>
<td>3.8 +/-7.2</td>
<td>3.8 +/-13</td>
</tr>
<tr>
<td>Low Fat</td>
<td>-1.2 +/-1.6</td>
<td>-17.3 +/-15.8</td>
<td>-5.9 +/-70.0</td>
<td>1.8 +/-7.7</td>
<td>-25.1 +/-25.3 *</td>
</tr>
</tbody>
</table>
Effects of decreasing sugar-sweetened beverage consumption on body weight in adolescents: A randomized controlled pilot study

Ebbeling CB et al                                  Pediatrics 2006;117:673-80

- 103 adolescents who regularly consumed SSBs were randomly assigned to non-caloric beverage consumption via home delivery vs control
- SSB consumption decreased 82% in the intervention group with no change in controls
- Change in BMI was 0.07 +/- 0.14 kg/m² for INT and 0.21 +/- 0.15 kg/m² for CON (ns)
- However, for subjects in the upper BMI tertile at baseline, BMI differed significantly between INT and CON: -0.64 +/- 0.23kg/m² vs +0.12 +/- 0.26 kg/m²
Dietary Composition Treatment of Obesity/ Dyslipidemia

• In adults with high TG, a low carbohydrate, high fat diet (40% carbohydrate/ 39% total fat/8% sat fat, 15% MUFA) results in a mean decrease in TG of 63% and a mean increase in HDL of 8%

• In 21 month old children with severely elevated TG, limiting simple sugar and carbohydrate intake resulted in a fall in TG from 274 +/-13.1 mg/dl at baseline to 88.8 +/-13.3 mg/dl after 12 months
Small Changes in Dietary Sugar and Physical Activity as an Approach to Preventing Excessive Weight Gain: The America on the Move Study

Rodearmel SJ et al

- 192 families with \( \geq 1 \) child with BMI \( \geq 85^{th} \) percentile; aged 7-14 yrs; randomized to AOM (n=100) or self-monitoring (n=92)

- AOM:
  1. Eliminate 100 kcal/d by replacing dietary sugar with non-caloric sweetener;
  2. Walk an additional 2000 steps/d above baseline, as measured by pedometers.

- Self-monitoring: Use pedometer to record physical activity

- GOAL: To reduce excessive weight gain in overweight children.
RESULTS

- AOM target children had significantly more steps/d than SM children (p<.05)
- AOM target children reported meeting 100 kcal sugar reduction goal on 78% of study days
- After 6 m, both groups showed significant decreases in BMI for age, greater in AOM but not statistically significant
- Significantly higher % of AOM target children maintained or reduced BMI-for-age
- AOM target children had consistently lower % with increased BMI-for-age
GLYCEMIC INDEX

- Glycemic Index (GI) = measure of the blood glucose response to a 50 gm portion of a selected carbohydrate
- Glycemic load = mathematical product of GI X carb amount
EFFECTS OF A LOW-GLYCEMIC LOAD vs LOW FAT DIET IN OBESE YOUNG ADULTS

- 73 obese young adults, aged 18 – 35 yrs
- Randomized to diets with low glycemic load (LGL) (40% carbohydrate/ 35% fat) vs low fat (LF) (55% carbohydrate/ 20% fat)
- No limitation of calories in either group
- 6 month intensive intervention followed by 12 month follow-up
- Baseline and 6m, 12m & 18m weight, body fat, BMI, fasting lipids and serum insulin (30 mins after a 75-g dose of oral glucose)
RESULTS

• **LGL**: Glycemic load decreased by 19.8 g/1000 kcal; fat increased 3 +/- 1.3% of energy; no change in sat fat

• **LF**: Total fat intake decreased -10.8 +/- 1.3% of kcals; sat fat decreased -4.5 +/- 0.6%; glycemic load increased by 5.0 +/- 2.5 g/1000 kcal.
RESULTS

- Weight loss did not differ between groups (~4.5 kg at 6m, ~2kg at 18 m)
- For LGL group, high baseline insulin subgroup had significantly greater weight loss than those on LF diet (-5.8 vs -1.2 kg)
- Subjects with high baseline insulin had higher TG (130+-105 mg/dl vs 102+-59)
- At 6m: TG decreased 21.2% in LGL vs 4% in LF
  LDL decreased 16.3% in LF vs 5.8% in LGL
  HDL increased 1.6% in LGL vs -4.4% in LF
- At 18 m, decreases in LDL-C in LF group and increase in HDL in LGL group persisted; TG were lower in LGL group but not significantly.
- Baseline insulin differences did not affect lipid changes
METABOLIC SYNDROME
ATP-III Definition
>=3 of these factors:

- Central/ abdominal adiposity: Waist circumference (WC) >102 cm (men), >88 cm for women
- Type 2 diabetes
- Dyslipidemia (High TG, low HDL-C)
- Blood pressure >130/85 or treated hypertension
- Metabolic syndrome is seen in at least 39% of adults, including 7% of men and 6% of women in the 20- to 30-year-old age group.

METABOLIC SYNDROME IN CHILDHOOD

- No established definition in children
- Met S “cluster” with hyperinsulinemia added to T2DM category is prevalent
- From NHANES 1999 to 2002, prevalence estimates for Met S for all teens from 2.0-9.4% and for obese teens from **12.4-44.2%**.
- From the Princeton study, Met S cluster at 6 – 19 yrs of age in 1973-1976 was a significant predictor of both the metabolic syndrome in adult life and of cardiovascular disease events at follow-up 25 years later.

DIETARY SUGAR/SSB AND METABOLIC SYNDROME

• Re: SSB intake and Met Syn:
  - In the Framingham Offspring Study, individuals who consumed \( \geq 1 \) SSB/d had a 39% greater risk of developing the Met Syn over 4 yr follow-up when compared with non-consumers.

• Re: SSB intake and T2DM:
  - Follow-up of >50,000 women X 8 yrs demonstrated that those consuming \( \geq 1 \) SSB/d had an 83% greater risk of developing T2DM. The difference was significant even after correction for BMI.
    Schulze MB et al. JAMA 2004;292:927-934

  - Follow-up of >70,000 women X 18 yrs showed that after correction for BMI and energy intake, women who consumed 2-3 SSBs/day had a 31% greater risk for T2DM than those who consumed <1SSB/mo.
    Bazzano LA et al. Diabetes Care 2008;31:1311-1317

• No studies like this in children.

Metabolic Syndrome: Suggested Mechanisms Linking Components

SUMMARY

• Taste preference for sweetness is present from birth and is reinforced by early diet experiences
• Preference for high sugar diet choices tracks from early childhood into adult life
• High dietary sugar is associated with development of CV risk factors, beginning in childhood (Obesity, high BP, dyslipidemia, metabolic syndrome cluster)
• Underlying biologic mechanisms not clearly defined but negative effect appears to be mediated by the association with obesity
• Limited number of intervention trials reducing added sugar intake show improved CV risk profile
• More research needed