Childhood Asthma, Obesity and Western Diet: Complex interactions and possible solutions

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NIEHS

EPA
The percentage of the U.S. population with asthma increased from 3.1% in 1980 to 5.5% in 1996 and 7.3% in 2001 to 8.4% in 2010.
Current Asthma Prevalence for Youth by Race/Ethnicity, Ages 5-17, 2005-2007

10.1% Overall

- Non-Hispanic Black: 14.2%
- Non-Hispanic White: 9.1%
- Hispanic: 10%
- Asian: 7.1%
- American Indian / Alaska Native: 10.2%
Many Factors Coalesce Unfavorably in Inner City

- Education
- Health Care Access
- Ambient Air Pollution
- Poverty
- Occupation
- Allergens
- Indoor Pollution
- Diet
- Obesity
Figure 2. Trends in overweight, obesity and extreme obesity, ages 20-74 years

Note: Age-adjusted by the direct method to the year 2000 US Bureau of the Census using age groups 20-39, 40-59 and 60-74 years. Pregnant females excluded. Overweight defined as 25≤BMI<30; obesity defined as BMI≥30; extreme obesity defined as BMI≥40.
Dietary Change in the U.S.

The Rise of Commercially Prepared Food

- Percent of total food spending


- Other away from home
- Fast food
- Home

USDA Economic Research Service
Change in U.S. Diet

↑ INTAKE
• Processed foods (refined grains, meats, “fast foods”)
• High fat foods, n6-PUFAs
• Sugar-enriched desserts and drinks

↓ or stable INTAKE
• Whole grains, poultry, fruits and vegetables
• Low fat foods, n-3 PUFAs, antioxidants

Observational evidence that Diet impacts Asthma

• Nutrients (e.g., vitamins C, D, E, ω-3 fatty acids)
  (Allan et al., Am Diet Assoc 2009)

• Foods (e.g., fruit, vegetables, and fish)
  (Nurmatov et al., J Allergy Clin Immunol 2011)

• Dietary patterns (e.g., Mediterranean diet)
  (Lv et al., J Asthma Allergy 2014)

• Western Diet pattern (e.g. high processed meat)
  (Brigham al., Annals Allergy Asthma Immunol 2015)

Categories of Weight

- Normal: BMI 18.5 – 24.9
- Overweight: BMI 25 – 29.9
- Obese: BMI 30 – 34.9
- Severely Obese: BMI 35 – 39.9
- Morbidly Obese: BMI ≥ 40

(*BMI ≥ 30)

Source: CDC Behavioral Risk Factor Surveillance System.
BMI and asthma prevalence in children and young adults NHANES

Visness et al. J Asthma 2010
>30,000 children ages 2 to 14 years

Overweight and obese compared to normal weight:

- Increased symptoms in response to \( \text{NO}_2 \) and \( \text{PM}_{10} \)
- Increased risk of doctor diagnosed asthma in response to \( \text{SO}_2 \) and \( \text{PM}_{10} \)

Effect of body size on breathing pattern and fine particle deposition in children

Particle deposition was 2.8 times greater in overweight compared to leanest children.

*Relationships were significant after adjusting for height, and age.
Potential Mediators of Susceptibility

- Differences in particle deposition due to differences in breathing patterns\(^5\)
- Enhanced oxidative stress and inflammatory response to pollutant exposure\(^{1-4}\)
- Enhanced hyperresponsiveness related to adipokines
- Corticosteroid resistance with increased weight\(^6\)
- Differential prevalence in comorbidities\(^7\)

Diet and Obesity Modify the Response to Inhaled Allergens and Pollutants

- Diet
- Obesity
- Allergens
- Pollutants
- Inflammation
- Oxidative Stress
- Symptoms
  - Lung function
  - Medication use
## Major Dietary Sources of Energy

<table>
<thead>
<tr>
<th>Food</th>
<th>% of Energy</th>
<th>5-8 yrs</th>
<th>% of Energy</th>
<th>9-13 yrs</th>
<th>% of Energy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk</td>
<td>13.9</td>
<td></td>
<td>Chips</td>
<td></td>
<td>10.1</td>
</tr>
<tr>
<td>Pizza</td>
<td>7.9</td>
<td></td>
<td>Pizza</td>
<td></td>
<td>9.1</td>
</tr>
<tr>
<td>Chips</td>
<td>7.7</td>
<td></td>
<td>Rice &amp; Pasta</td>
<td></td>
<td>7.4</td>
</tr>
<tr>
<td>Sweetened Drinks</td>
<td>7.5</td>
<td></td>
<td>Chicken</td>
<td></td>
<td>6.0</td>
</tr>
<tr>
<td>Cereals</td>
<td>7.1</td>
<td></td>
<td>Cereals</td>
<td></td>
<td>5.7</td>
</tr>
<tr>
<td>Breads</td>
<td>5.5</td>
<td></td>
<td>Milk</td>
<td></td>
<td>5.6</td>
</tr>
<tr>
<td>Sandwich/Burger</td>
<td>5.2</td>
<td></td>
<td>Meat</td>
<td></td>
<td>5.3</td>
</tr>
<tr>
<td>Chicken</td>
<td>5.1</td>
<td></td>
<td>Soda</td>
<td></td>
<td>4.8</td>
</tr>
<tr>
<td>Sweetened juices</td>
<td>3.9</td>
<td></td>
<td>Sweetened Drinks</td>
<td></td>
<td>4.8</td>
</tr>
<tr>
<td>Meat</td>
<td>3.6</td>
<td></td>
<td>Sandwich/Burger</td>
<td></td>
<td>4.7</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>67.3</strong></td>
<td></td>
<td><strong>Total</strong></td>
<td></td>
<td><strong>63.4</strong></td>
</tr>
</tbody>
</table>

# Intake of Energy & Selected Nutrients: Boys 5-8 yrs

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Median</th>
<th>DRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy (kcal)</td>
<td>2097</td>
<td>1600</td>
</tr>
<tr>
<td>Dietary Fiber (g)</td>
<td>13.1</td>
<td>25</td>
</tr>
<tr>
<td>Saturated Fat (g)</td>
<td>29.6</td>
<td>As low as possible</td>
</tr>
<tr>
<td>Monounsaturated Fat (g)</td>
<td>15.1</td>
<td></td>
</tr>
<tr>
<td>Polyunsaturated Fat (g)</td>
<td>8.5</td>
<td></td>
</tr>
<tr>
<td>Omega 3 FA (g)</td>
<td>0.5</td>
<td>1.2</td>
</tr>
<tr>
<td>Omega 6 FA (g)</td>
<td>7.4</td>
<td>1.2</td>
</tr>
<tr>
<td>Potassium (mg)</td>
<td>1974</td>
<td>3800</td>
</tr>
<tr>
<td>Sodium (mg)</td>
<td>3144</td>
<td>1200</td>
</tr>
</tbody>
</table>

Adequate: Folate, B-12, Iron, Calcium, Vitamin C and D

DRI: Dietary Reference Intake, using Adequate Intake and Recommended Daily Allowance
Dietary Interventions in Asthma

Mediterranean type diet, Derived from DASH

Higher unsaturated fat
From

Olive oil
Canola oil
Safflower oil
Nuts and seeds

Follow the DASH diet to potentially lower your blood pressure.
Study Design

Omni Heart

Control Diet

4 week washout

Control Diet

0

-urine
-eNO
-blood
-nasal lavage
-nasal epithelial cells
--symptoms/PFT

2 weeks

-urine
-eNO
-blood
-nasal lavage
-nasal epithelial cells
--symptoms/PFT

4 weeks

-urine
-eNO
-blood
-nasal lavage
-nasal epithelial cells
--symptom/PFT
Sample menu from OmniHeart

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
</table>
| **Breakfast** | Orange juice  
                  Cereal with raisins, skim milk  
                  White bread toast with olive oil margarine and jelly |
| **Lunch**  | Chicken sandwich: white bread, chicken breast, barbeque sauce, olive oil margarine  
                  Olive oil potato chips  
                  Spinach salad with tomato and olive oil balsamic dressing  
                  Broccoli salad with safflower oil  
                  Tomato juice |
| **Dinner** | Black bean taco: black beans with vegetables,  
                  3-grain pilaf with olive oil*  
                  Tortilla chips  
                  Carrots, cooked  
                  Pecan cookie  
                  Skim milk |
| **Snack**  | Mandarin oranges  
                  Almonds |

Appel LJ et al. JAMA 2005; Carey VJ et al. Clinical Trials 2005
Changes in report of dietary intake

Changes in Serum Caretenoids

Change in Alpha Carotene

Change in Lutein

\( p=0.04 \)

\( p=0.01 \)
Changes in Asthma Outcomes

Change in Asthma Control Test Scores

Changes in Lung Function

1.0
0.5
0
-0.5
-1.0

control intervention

10
5
0
-5

control intervention
Nrf2-Keap1 System

Environmental allergens (ROS, inflammatory agents)

Keap1

Nrf2

Keap1

Nrf2

Environmental stress response
- Glutathione biosynthesis
- NADPH synthesis
- Antioxidants enzymes
- Proteasomal system
- Scavenger receptors
- Antimicrobial defenses
- Antiinflammatory defenses

...our major cellular defense against oxidative stress
Cruciferous vegetables

- Broccoli sprouts*  
  *Brassica oleracea*
- Cabbage
- Cauliflower
- Bok choy
- Kale
- Collard greens
- Chinese broccoli
- Kohlrabi
- Mustard
- Turnip
- Radish
- Arugula
- Watercress
- Broccoli raab

Cruciferous vegetables belong to the family of plants “Cruciferae” and genus “Brassicaceae"
Activators of Nrf2

SA1.1: Oral activation of Nrf2
SA1.2: Specific effects during challenge
SA1.3: Specific effects during sensitization

Omega-3 Fatty Acids
Docosahexaenoic acid (DHA)

Omega-3 fatty acids are found in oily fish like salmon and flaxseed and canola oils

Genetic activation of Nrf2, via Keap1 deletion in airway epithelium, dendritic cells and CD4 T cells

Aim 1

Aim 2

Aim 3

Inflammation
Cytokines
AHR
Mucus

A

Saline

OVA
Nrf2-deficiency increases allergic asthma

Rangasamy et al., JEM 2005
Feeding Nrf2 activator, TMC, reduces asthma
Genetic activation of Nrf2 reduces asthma

Buffalo Chicken Wrap

Seafood Salad Wrap
Salad made of sweet crab meat, real shrimp, celery, onion, and mayonnaise - all wrapped up in a sandwich wrap.

Tuna Salad Wrap
Creamy tuna salad made with onion, celery, pickle relish and mayonnaise. Just like mom used to make!

Buffalo Ranch Chicken Wrap
Spicy buffalo ranch sauce with bacon over crispy chicken with lettuce, celery, and tomatoes. Served with extra hot sauce on the side.

Barbeque Chicken Wrap
Crispy chicken smothered in sweet and tangy barbeque sauce with lettuce. Extra barbeque sauce on the side.

Beef Tacos
4 crunchy taco shells served with taco beef and nacho cheese, with diced tomato garnish. Sour cream and taco sauce served on the side.

Please choose one lunch item for each day of the week. Your choices will be repeated for the second week.
### Sulforaphane and Induction of Phase II Enzymes in Respiratory System

<table>
<thead>
<tr>
<th>BS Dose (homogenate form)</th>
<th>H0-1 (mean % change)</th>
<th>NQO1 (mean % change)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25g</td>
<td>4.43</td>
<td>-2.17</td>
</tr>
<tr>
<td>100g</td>
<td>15.32</td>
<td>13.86</td>
</tr>
<tr>
<td>125g</td>
<td>37.8</td>
<td>53.32</td>
</tr>
<tr>
<td>150g</td>
<td>105.1</td>
<td>142.19</td>
</tr>
<tr>
<td>175g</td>
<td>106.6</td>
<td>160.19</td>
</tr>
<tr>
<td>200g</td>
<td>120.9</td>
<td>198.8</td>
</tr>
</tbody>
</table>

Daily ingestion of BSH prepared from fresh BS 3 days
Gene expression from nasal lavage performed 2 hours after last BSH dose

OBesity Enhances Susceptibility to Pollutant Effects in Asthma (OBESE ASTHMA)

Consultants
P. N. Breysse

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N. N. Hansel
G. B. Diette
Administrative Core Staff

Executive Committee
Project Leaders and Core Leaders

External Advisory Committee

Community Outreach and Translational Core

Community Advisory Board

Project 1 – M. C McCormack & N.N. Hansel
Obesity as a susceptibility factor to PM$_{2.5}$ in children with asthma

Project 2 - E. C. Matsui & K. Koehler
Novel exposure metrics for ultrafine PM in children with asthma

Project 3 – S. Polotsky & W. Mitzner
Role of obesity in biological responses to PM in mice

Obesity as a susceptibility factor to pollution exposure in asthma - Organizational Chart
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