PHENYLKETONURIA

Debbie Galo
What it is PKU?

- 1934
- Metabolic disorder (chromosome 12)
  - Autosomal recessive

Deficiency of enzyme Phenylalanine Hydroxylase (PAH)
  - Cannot convert phenylalanine to tyrosine
- More than 500 mutations that can cause it
- Missense mutations (62%) of PAH alleles
  - Deletions, splicing defects, nonsense mutations, insertions, nonsense mutations, silent polymorphins
Normal Reaction of Phenylalanine

Phenylalanine → Tyrosine

**Chemical Reaction**

Phenylalanine + $\text{phenylalanine hydroxylase}$ $\rightarrow$ Tyrosine + $\text{tetrahydrobiopterin} + \text{dihydrobiopterin} + \text{H}_2\text{O} + \text{O}_2$

**Diagram**

- **Phenylalanine (Phe)**
- **Tyrosine (Tyr)**
- **Free Phe** and **Free Tyr**
- **Phe Tracer**
Phenylketonuria (PKU)
Types of PKU

- **Classic**
  - Dietary tolerance of Phe less than 350-400 mg per day
  - Residual activity of PAH(enzyme) is less than 5%

- **Moderate or Mild**
  - Dietary tolerance of Phe less than 350-600 mg per day
  - Residual activity of PAH is less than 10%

- **Benign**
  - No dietary restrictions of Phe but residual activity of PAH is less than 15%

- **No cure**
How PKU affects the body

- Toxicity in the blood
- Tyrosine deficiency
- Brain development
- Tyrosine to L-Dopa
How PKU affects the body

- Untreated children:
  - Visual Cues
  - Nervous system damage
  - Low levels of Phe
  - Pregnant mothers
  - Other Symptoms
Demographics

- 1 in 10,000-20,000 depending on the country
  - United States
    - 1 in 10,000 to 1 in 20,000-US (Caucasian and Asian)
    - Less in African Americans
  - Ireland
  - Finland
  - Turkey
  - Iran
  - Poland and Czech Republic
  - Equal in males and females
Diagnosis

- PKU treatment programs
- Blood sample between 12-28 hours after birth
- Heel of the foot
Treatments

- Early diagnosis and controlling diet
- Large neutral amino acids
- GMP (glycomacropeptide)
- Kuvan (Sapropterin di-hydrochloride)
  - Tetrahydrobiopterin or BH4 is the cofactor
- Other treatments
Treatments

- **Diet control**
  - Liberal or strict
  - Recommended to continue for life
  - Developed in the 1960’s
  - Eliminates all high protein foods
  - Formula for all ages
  - ‘Challenge’
  - Reintegration=challenging

- **Patient’s Responsibility**

- **Dietitian’s Responsibility**
How the body is affected

- IQ
- Cardiovascular Disease
- Osteopenia
### Phenylalanine Content

<table>
<thead>
<tr>
<th>Food</th>
<th>Amount</th>
<th>Phenylalanine content</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry low-protein spaghetti</td>
<td>½ cup</td>
<td>5 mg</td>
</tr>
<tr>
<td>Whole medium apple</td>
<td>One</td>
<td>9 mg</td>
</tr>
<tr>
<td>Fresh whole medium pear</td>
<td>One</td>
<td>17 mg</td>
</tr>
<tr>
<td>Tortilla chips</td>
<td>3 chips</td>
<td>25 mg</td>
</tr>
<tr>
<td>Cooked green beans</td>
<td>½ cup</td>
<td>34 mg</td>
</tr>
<tr>
<td>Baked potato</td>
<td>¼ cup</td>
<td>36 mg</td>
</tr>
<tr>
<td>Whole medium banana</td>
<td>One</td>
<td>43 mg</td>
</tr>
<tr>
<td>Regular cooked spaghetti</td>
<td>¼ cup</td>
<td>81 mg</td>
</tr>
<tr>
<td>Wonder bread, white</td>
<td>One slice</td>
<td>105 mg</td>
</tr>
<tr>
<td>Frosted Mini wheats</td>
<td>4 biscuits</td>
<td>115 mg</td>
</tr>
<tr>
<td>Honey-dipped donut</td>
<td>One</td>
<td>125 mg</td>
</tr>
<tr>
<td>Corn on the cob</td>
<td>One ear</td>
<td>212 mg</td>
</tr>
<tr>
<td>Peanut butter</td>
<td>One tbsp.</td>
<td>244 mg</td>
</tr>
<tr>
<td>Burger King onion rings</td>
<td>One serving</td>
<td>250 mg</td>
</tr>
<tr>
<td>Cheddar cheese</td>
<td>One ounce</td>
<td>372 mg</td>
</tr>
<tr>
<td>McDonald’s hamburger</td>
<td>One</td>
<td>624 mg</td>
</tr>
<tr>
<td>Arby’s bacon/egg croissant</td>
<td>One</td>
<td>870 mg</td>
</tr>
<tr>
<td>High Phenylalanine Foods:</td>
<td>Low Phenylalanine Foods:</td>
<td></td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>--------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Fish</td>
<td>Most Fruit</td>
<td></td>
</tr>
<tr>
<td>Beans</td>
<td>Most Vegetables</td>
<td></td>
</tr>
<tr>
<td>Diet Soda</td>
<td>Sugars</td>
<td></td>
</tr>
<tr>
<td>High-Protein Foods</td>
<td>Special Breads, Cookies, Crackers</td>
<td></td>
</tr>
<tr>
<td>Wheat</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dairy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meat</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nuts &amp; Legumes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eggs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High Phenylalanine Foods</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low Phenylalanine Foods</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# Financial Responsibility

<table>
<thead>
<tr>
<th>Food</th>
<th>Low Protein*</th>
<th>Regular</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bread (24 oz.)</td>
<td>$ 7.02</td>
<td>$ 1.99</td>
</tr>
<tr>
<td>Spaghetti (16 oz.)</td>
<td>$ 5.23</td>
<td>$ 0.95</td>
</tr>
<tr>
<td>Flour (5 lbs.)</td>
<td>$ 13.75</td>
<td>$ 1.49</td>
</tr>
<tr>
<td>Chocolate Chip Cookies (6 oz.)</td>
<td>$ 2.95</td>
<td>$ 1.13</td>
</tr>
<tr>
<td>Rice (28 oz.)</td>
<td>$ 12.33</td>
<td>$ 2.89</td>
</tr>
<tr>
<td>Gelatin Dessert (3 oz.)</td>
<td>$ 1.34</td>
<td>$ 0.59</td>
</tr>
</tbody>
</table>
Blood levels

- Keep it between 2-10mg/dL
- 2-6mg/dL during pregnancy

- How many (g) per day can they eat?
Metabolic Syndrome in Children and Adolescents with Phenylketonuria

**Management**
- Diet free of animal protein and with restricted vegetable protein consumption

**Issue**
- Protein restriction causes the consumption of carbohydrate-rich food and lipids in particular, increasing the risk of weight gain
- A study shows that PKU patients with excess weight are vulnerable to the development of metabolic syndrome.
Cont.

- Participant: 58
  (29 patients with excess weight and 29 patients with normal weight)
- Age: 4-15
- Method:
  As for the laboratory tests, patients underwent a 10-hour fast, with a maximum 14 hours of fasting. Serum concentrations of fasting phe, total cholesterol (TC), HDL cholesterol, triglycerides, glucose and basal insulin were determined.
## Results

### Relation to blood phe control

<table>
<thead>
<tr>
<th>Variable</th>
<th>Excess weight</th>
<th>Normal weight</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequate blood phe control</td>
<td>58.6%</td>
<td>41.4%</td>
<td>0.14</td>
</tr>
</tbody>
</table>
Results

- Blood levels of total cholesterol and HDL cholesterol, triglycerides, blood glucose, and basal insulin in phenylketonuria patients with excess weight and normal weight

<table>
<thead>
<tr>
<th>Variables</th>
<th>Excess weight</th>
<th>Normal weight</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td>136.2 (± 22.2)</td>
<td>130.7 (± 20.2)</td>
<td>0.32</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dL)</td>
<td>34.0 (± 7.5)</td>
<td>37.0 (± 8.0)</td>
<td>0.00</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>109.0 (± 43.0)</td>
<td>74.0 (± 40.5)</td>
<td>0.00</td>
</tr>
<tr>
<td>Glycemia (mg/dL)</td>
<td>73.8 (± 6.4)</td>
<td>76.3 (± 6.3)</td>
<td>0.13</td>
</tr>
<tr>
<td>Basal insulin (uUI/mL)</td>
<td>8.4 (± 8.95)</td>
<td>3.8 (± 5.15)</td>
<td>0.02</td>
</tr>
</tbody>
</table>
Comparison between total cholesterol/HDL-c, blood levels of basal insulin, and HOMA in phenylketonuria patients with excess weight and normal weight

<table>
<thead>
<tr>
<th></th>
<th>Excess weight</th>
<th>Normal weight</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total cholesterol/HDL-c</strong></td>
<td>4.00 (± 0.84)</td>
<td>3.33 (± 0.81)</td>
<td>0.00</td>
</tr>
<tr>
<td><strong>Insulin (uUI/mL)</strong></td>
<td>8.40 (± 8.95)</td>
<td>3.8 (± 5.15)</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>HOMA</strong></td>
<td>1.64 (± 1.59)</td>
<td>0.70 (± 1.10)</td>
<td>0.03</td>
</tr>
</tbody>
</table>
23 yr old female with a history of mild-to-moderate PKU was found to be 2 months pregnant

Diet controlled case study

Infant was born totally normal and with a heterozygous gene for PKU

Maternal PKU
Nutritional Consequences of Adhering to a Low Phe Diet for Late-Treated Adults with PKU

- **Background**
  - Late diagnosed patients with mild-severe mental retardation
  - The main treatment for PKU is a low-Phe diet, Phe-free protein substitute and low-protein special foods
  - The purpose of this study is to describe the dietary composition and nutritional status of late-diagnosed patients on the PKU diet.
Methods

- 19 late diagnosed PKU patients
  - Food diary (4 days)
  - Blood tests
  - Nutritional status
Results

- Total kcal range- 2,091 kcal/day median (1,537-3,277 kcals/day)
- Carbs – 59% of total intake (53-70%)
  - 15% from added sugar
  - 26% from fat
- Protein – 1.02 g/day (0.32- 1.36 g/day)
- Phe levels- 746 mg/day (360-1,370 mg/day)
- Excess iron, folate, and folic acid
Wiig, I., Motzfeldt, K., Løken, E., & Kase, B. (n.d.). Nutritional Consequences of Adhering to a Low Phenylalanine Diet for Late-Treated Adults with PKU. *JIMD Reports* *JIMD Reports - Case and Research Reports*, 2012/4, 109-116. cd


http://www.medhelp.org/lib/pku.htm

http://pkunews.org/about/intro.htm

http://npkua.org/Education/AboutPKU.aspx


http://pkunews.org/personal/parent.htm