Prevention of Spina Bifida & Anencephaly: The Importance of Folic Acid Fortification of Flour Assessing Effects Worldwide

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National Center on Birth Defects and Developmental Disabilities
Centers for Disease Control and Prevention
Outline

- Epidemiology of spina bifida and anencephaly (SBA) and folic acid
- Prevention of SBA through the use of folic acid
- Impact of folic acid fortification in reducing SBA in the U.S. and around the world
Spina bifida & Anencephaly

- Serious birth defects
  - spina bifida and anencephaly
- >1 of 1000 pregnancies
- > 300,000 yearly worldwide
- Increased consumption of folic acid can prevent 50 -70%
- Maternal folic acid levels need to be raised very early in pregnancy
- 50% of US pregnancies are unplanned
Lifelong disabilities of spina bifida

- Loss of sensation
- Paralysis of muscle groups
- Loss of bladder, and bowel control
- Learning and developmental issues
- Orthopedic problems
Causes of Spina Bifida and Anencephaly

**Before 1980’s**
- 90% unknown

**After 1980’s**
- 50%-70% folic acid-preventable
- 40% unknown

5% - 10% due to family history, maternal diabetes, antiepileptic medications, genetic conditions, etc.
<table>
<thead>
<tr>
<th>Studies</th>
<th>% reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>'80-Smithells</td>
<td>86%</td>
</tr>
<tr>
<td>'81-S. Wales</td>
<td>59%</td>
</tr>
<tr>
<td>'88-Atlanta</td>
<td>60%</td>
</tr>
<tr>
<td>'89-W. Australia</td>
<td>70%</td>
</tr>
<tr>
<td>'89-CA/Illinois</td>
<td>7%</td>
</tr>
<tr>
<td>'89-Boston</td>
<td>65%</td>
</tr>
<tr>
<td>'90-Cuba</td>
<td>100%</td>
</tr>
<tr>
<td>'91-UK-MRC</td>
<td>71%</td>
</tr>
<tr>
<td>'92-Hungary</td>
<td>100%</td>
</tr>
<tr>
<td>'93-New England</td>
<td>60%</td>
</tr>
<tr>
<td>'95-California</td>
<td>52%</td>
</tr>
<tr>
<td><strong>'99-P.R. China</strong></td>
<td><strong>80%</strong></td>
</tr>
</tbody>
</table>
1992 U.S. Public Health Service Folic Acid Recommendation to Prevent SBA

-400 micrograms (0.4mg) folic acid daily,
-for all women capable of becoming pregnant,
-to prevent spina bifida and other NTDs.
-Increase consumption of folic acid/folate:

• Improve dietary habits
• Take a daily folic acid supplement
• Consume fortified foods
Food vs. supplements

- Vitamin supplements
- "Natural" food folates
- Fortified foods
“Folate” is not equal to “Folic Acid”

Folate (food)
- Occurs naturally in many foods
- Not as bioavailable as folic acid

Folic acid (pills, foods)
- Synthetic form of ‘folate’
- Found in vitamin supplements, breakfast cereals, enriched flour, and enriched cereal-grain products
Dietary approach: to deliver folate to populations

**Advantages**
- Multiple benefits of healthy diet

**Disadvantages**
- Requires continuous public education
- Requires behavior change
- High cost of folate-rich foods
- Quantity, absorption and bioavailability

- U.S. women consume on average 200 mcg folate per day
For Example...

To get enough folate from food that equals 400 mcg of folic acid each day, a person would have to eat one of the following:

- 4 slices of fried beef liver
- 5½ cups of black beans
- 14½ cups of raw broccoli
- 44½ medium ripe tomatoes
- 17½ cups of orange juice
Vitamin Supplement approach:

**Advantages**
- Excellent bioavailability

**Disadvantages**
- Continuous public education
- Behavior change
- Relative high cost of tablets

- Most U.S. MV supplements contain 400 mcg FA
- ONLY 25% - 30% U.S. women consume 400 mcg FA/day
Percent women taking vitamins with folic acid daily

All women age 18-45, 1995 - 2005

28% 32% 32% 34% 29% 33% 32% 40% 33%

1995 1997 1998 2000 01 02 03 04 05
Food fortification approach:

**Advantages**
- Good bioavailability
- Cost low
- Almost 100% coverage
- Convenient; minimal behavior change

**Disadvantages**
- Amount added to foods limits effectiveness.

- U.S. women consume on average 130 mcg folic acid per day
What Approaches Work?
What is the best way to get Folate / Folic Acid?

- Diet….natural foods, vegetables, fruits, beans, yeast, liver
- Pills…..” folic fcid supplements,” “dietary supplements”
- Fortification…FA added to foods: flour, rice, pasta breakfast cereals
Consumption of Folic Acid & Dietary Folate: Effect on Red Cell Folate, Ireland 1996.

<table>
<thead>
<tr>
<th>Intervention method</th>
<th>Red Blood Cell Folate, % change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dietary advice</td>
<td>+ 16%, NS</td>
</tr>
<tr>
<td>Diet natural folate</td>
<td>+ 11%, NS</td>
</tr>
<tr>
<td>400 mcg folate</td>
<td></td>
</tr>
<tr>
<td>Supplement</td>
<td>+ 40%, p&lt;0.05</td>
</tr>
<tr>
<td>400 mcg Folic Acid</td>
<td></td>
</tr>
<tr>
<td>Fortified food</td>
<td>+ 52%, p&lt;0.05</td>
</tr>
<tr>
<td>400 mcg Folic Acid</td>
<td></td>
</tr>
</tbody>
</table>

Cuskelley et al., Lancet; 1996.
Folate Folic Acid Delivery Methods

- Diet....natural foods, vegetables, fruits, beans, yeast, liver
- Pills.....” FA supplements,” “dietary supplements”
- Fortification...FA added to foods: flour, rice, pasta breakfast cereals
Worldwide flour fortification programs

Source: FFI website, June 2007
<table>
<thead>
<tr>
<th>Country</th>
<th>Food types</th>
<th>Folic acid ppm</th>
<th>mcg folic acid (design)</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA, 1998</td>
<td>Wheat, corn flours, rice, pasta</td>
<td>1.4 ppm</td>
<td>100 mcg</td>
</tr>
<tr>
<td>Canada, 1998</td>
<td>Wheat, corn flours, rice, pasta</td>
<td>1.5 ppm</td>
<td>100 mcg</td>
</tr>
<tr>
<td>Costa Rica, 1998</td>
<td>Wheat, corn flours, rice, milk</td>
<td>1.8 ppm</td>
<td>100 mcg</td>
</tr>
<tr>
<td>Chile, 2000</td>
<td>Wheat flour for bread</td>
<td>2.2 ppm</td>
<td>400 mcg</td>
</tr>
</tbody>
</table>
Evaluation and monitoring of flour fortification with folic acid to prevent spina bifida and anencephaly

Blood folates
SBA prevalence rates
Cost benefit analyses
Median serum and red blood cell folate levels, before and after folic acid fortification, NHANES, non-pregnant women, 15-44 years

United States

<table>
<thead>
<tr>
<th></th>
<th>Serum folate</th>
<th>Red blood cell folate</th>
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</thead>
<tbody>
<tr>
<td><strong>before</strong></td>
<td>4.8 ng/mL</td>
<td>157 ng/mL</td>
</tr>
<tr>
<td><strong>after</strong></td>
<td>13.0 ng/mL</td>
<td>255 ng/mL</td>
</tr>
</tbody>
</table>

Serum folate changes in the Americas before and after folic acid fortification

<table>
<thead>
<tr>
<th>Country</th>
<th>Before Fortification</th>
<th>After Fortification</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td>4.8 ng/mL</td>
<td>13.0 ng/mL</td>
</tr>
<tr>
<td>Newfoundland</td>
<td>6.0 ng/mL</td>
<td>8.0 ng/mL</td>
</tr>
<tr>
<td>Costa Rica</td>
<td>4.3 ng/mL</td>
<td>16.4 ng/mL</td>
</tr>
<tr>
<td>Chile</td>
<td>10.1 ng/mL</td>
<td>15.8 ng/mL</td>
</tr>
</tbody>
</table>
Change in U.S. NTD prevalence by fortification status, per 10,000, NBDPN, 24 surveillance programs

- Spina bifida
- Anencephaly

Pre-fortification
Optional fort.
Mandatory fortification

26%
NTD Prevalence changes in the Americas before and after folic acid fortification

Rates per 10,000 live births

Before fortification
After fortification

USA: 10.6 - 7.6
Canada: 15.8 - 8.6
Costa Rica: 9.7 - 6.3
Chile: 17.0 - 10.1

-26% - 46% - 35% - 41%
Decrease in the number of SBA-affected pregnancies in the United States per year, NBDPN

Number of NTD-affected pregnancies

Before fortification 1995-1996
After fortification 1999-2000

Source: National Birth Defects Prevention Network, includes prenatal ascertainment of cases
United States
Economic Evaluation of Folic Acid Fortification

In 1998 U.S. fortified wheat flour at 140 mcg/ 100g flour
- Reduction in NTDs -- 26%

- Cost of fortification $3 million per year ($1)
- Direct cost averted $125 million per year ($40)

Chile

Economic Evaluation of Folic Acid Fortification

In 1998 Chile fortified wheat flour at 220 mcg/100g flour

- Reduction in NTDs -- 41%

- Cost of fortification $0.2 million per year ($1)
- Direct cost averted $2.2 million per year ($11)

Llanos, Hertrampf, Pardo, Grosse, and Uauy (Health Policy, 2007)
Evaluation and monitoring of flour fortification with folic acid to prevent spina bifida and anencephaly

Blood folates
SBA prevalence rates
Cost benefit analyses

cost savings

↑
↓
+
Evaluation of the change in SBA prevalence, U.S.

<table>
<thead>
<tr>
<th>Actual - SBA</th>
<th>Goal - SBA</th>
</tr>
</thead>
<tbody>
<tr>
<td>% decline</td>
<td>% decline</td>
</tr>
<tr>
<td>26%</td>
<td>50%-70%</td>
</tr>
<tr>
<td>1,000</td>
<td>2,000</td>
</tr>
</tbody>
</table>
Evaluation of the change in SBA prevalence, U.S.

Actual - SBA
26% decline
1,000

Since 1998, more than 11,000 babies have been born healthy, who would have either died or had serious disabilities.
Worldwide flour fortification programs

Source: FFI website, June 2007
Folic Acid-Preventable SBA in 2006
300,000 affected babies worldwide

Worldwide SBA

Not Prevented
Prevented

93%
7%
Conclusions:
Current Knowledge and Practical Applications: Flour Fortification

Adding folic acid to flour and bread:

- Blood folate levels have increased substantially
- Countries now report declines of SBA from 25% to 46%.
- Decreasing numbers of spina bifida and anencephaly are consistent with an increase in folic acid in fortified flour and foods.
Conclusions (cont’d)

Adding folic acid to flour and bread:

- Fortification of foods with folic acid is feasible, effective and safe. It is excellent public health policy.

- At the present time, there are no proven adverse effects of folic acid fortification.

- The economic benefit in preventing SBA exceeds the costs of implementing food fortification efforts with folic acid.
U.S. National Folic Acid Campaign to Prevent Birth Defects

Folic Acid → Healthy Babies