Preventing Folic Acid Preventable Spina Bifida and Anencephaly—25 Years On

International Federation for Spina Bifida and Hydrocephalus
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Lyall Thurston

- I dedicate my talk to him
- New Zealand, parent champion par excellence for care AND prevention
- Prime reason flour fortified in Australia
- Prime Minister in New Zealand prohibits implementation of regulations for fortification
Overview

• Good News!
  – Preventing \textbf{35,000} (15\%) children from folic acid preventable spina bifida and anencephaly—350,000 in last 10 years

• Bad News!
  – \textbf{200,000} children each year (20 times the number of thalidomide babies) are born with folic acid preventable spina bifida and anencephaly—2,000,000 last 10 years

• Opportunity
  – We know how to prevent all folic acid preventable spina bifida and should do it as fast as we can.
  – I look forward to working with you all to get full prevention done
Turning Point: 1991

• June 24, 1991, 5 p. m.

• Boca Raton, Florida
BeercRaton Resort and Club

NICK'S MARKET
- WINE
44-71. 8668 52-338
7-00 - 011 -
305 NICK

NICK
- NRC VIs
cold spot
- Fortified 72% Port
- No specialty VIs

Recent to Gomer Powell

Dose Issue
Cold refusen Dose
Testing cold - less - can't dry 40 mg
We Can ACHIEVE total prevention of SBA F Globally!

- Evidence-based intervention
- Reliable
- Inexpensive
- Cost-Effective
- Safe
- Sustainable

Preventing SBA F can reduce infant mortality by 5% to 10%
FDA Requires Folic Acid Fortification

• Required by Jan 1, 1998—6.5 years after the science
• Immediate increase in blood folates
• Immediate reduction in spina bifida and anencephaly to non folic acid preventable rate of 1 in 2000 births
• Immediate prevention of folate deficiency anemia
Good News

• We do not need any more research to prevent most of spina bifida in the world

• Folate deficiency - main cause of spina bifida

• Not multi-factorial: known causes—folate deficiency, valproic acid, maternal diabetes, arsenic (?), and unknown causes

• Unknown and other causes small proportion compared just to folate deficiency caused spina bifida

• We can prevent **ALL** folic acid preventable spina bifida by mandatory folic acid fortification!!!
Fortification Saves Money

• 20 to 150 US dollars saved in health care costs for every US dollar spent on fortification

• Money **SAVED** by fortification can be used to:
  – Improve care for children with spina bifida
  – Sustain, regulate, monitor fortification
  – Fund more costly prevention programs where needed such as supplements
2015 Status of Global Prevention of FAP SBA

Modest and High Prevention estimated using daily folic acid consumption of 100 mcg/day (range 20-150 mcg/day) and 200 mcg/day (≥151 mcg/day), respectively, from fortified wheat or maize flour.

Source: Center for Spina Bifida Research, Emory University (Accepted for Publication – Birth Defects Res Part A)
Bad News

• 200,000 each year in over 100 countries have folic acid preventable spina bifida and anencephaly because their government does not require folic acid fortification

• Each year 20 times as many children affected as were in all years damaged by thalidomide

• Last 10 years 2,000,000 children worldwide have been unnecessarily affected by folic acid preventable spina bifida or anencephaly
Sometimes, even if I stand in the middle of the room, no one acknowledges me.
Why Does No Country in Europe Require Folic Acid Fortification?
Mandatory Folic Acid Fortification is Safe!

- Mandatory folic acid fortification adds less than the Recommended Daily Allowance (RDA) of folic acid (~140 compared to 400 mcg/day)

- It is perfectly safe!
Spina Bifida Prevention Program

• Shared goal to triple prevention over 6 years

• IF, Center for Spina Bifida Prevention, Food Fortification Initiative, Taskforce on Global Health, Helen Keller-International, Project Health Children collaborating

• Seeking adequate funding from MacArthur Foundation Project 100&Change and others
Spina Bifida Prevention Program

• **Harness power** of parents and professional to get mandatory fortification

• Assist industry and governments to implement, regulate, and monitor progress towards total prevention

• Implement blood folate studies of women of reproductive age for rapid evaluation of fortification programs
IF Global Prevention Initiative

• Wonderful!!
• Create awareness of the need to prevent folic acid preventable spina bifida
• Parents and professional are powerful advocates globally and within each country
• Spina Bifida Prevention Project will assist as resources become available
Making Spina Bifida and Anencephaly More Visible

• Point out that folate deficiency is causing and has caused major epidemics of spina bifida and anencephaly

• Boston in 1930s

• China now

• Newfoundland before Canadian fortification
Unrecognized Epidemic of Spina Bifida and Anencephaly
China Folic Acid Community Intervention (Good Compliance)

Intervention = 400 mcg folic acid supplement daily

Berry et al. (1999) 341:1485-1490
NTD prevalence rates (per 1000 births) before and after fortification compared to China Community Trial of 400 mcg folic acid daily.
Making Spina Bifida and Anencephaly More Visible

• Show percent prevented by fortification is higher, the larger the epidemic
We Know the Rate of Non Folic Acid Preventable-Spina Bifida and Anencephaly

• 0.5 per 1000 births

• 1 in 2000 births

• 5 per 10,000 births
Non-Preventable Rate

- China supplement study
- Post fortification United States and Canada
- Post fortification case control studies no longer show protective effect of folic acid supplements because fortification is fully protective
- Modeling of spina bifida and anencephaly rates as a function of maternal red blood cell folate
Blood folate insufficiency, not deficiency, is the relevant measure for neural tube defect prevention.

http://www.who.int/nutrition/publications/guidelines/optimalserum_rbc_womenrep_tubedefects/en/
Epidemics of SBA F

- 1935 Boston
- 2014 North China
- 2014 India
- 1968 Atlanta
- 2014 Ukraine
- 2014 Africa
- 2014 USA/Canada (mandatory fortification 150 mcg per day)
- China study (400 mcg folic acid per day)
Reductions in the epidemic levels of SBA F through folic acid interventions

- 90% Reduction
- 80% Reduction
- 50% Reduction
Overview

• Good News!
  – Preventing 35,000 (15%) children from folic acid preventable spina bifida and anencephaly—350,000 in last 10 years

• Bad News!
  – 200,000 children each year still are born with folic acid preventable spina bifida and anencephaly—20 times thalidomide damaged babies each year and 2,000,000 last 10 years

• Opportunity
  – We know how to prevent all folic acid preventable spina bifida and should do it as fast as we can.
  – I look forward to working with you all to get full prevention done soon!!!
Non-Hispanic white seniors aged ≥60 yrs
NHANES, 2001–2002

Serum folate quintiles and their geometric means (nmol/L)

Berry, RJ et al. (2007). AJCN; 85:265-7
The End
PCV UPTAKE FASTEST EVER IN LOW Income countries

Percentage of countries that have universally introduced vaccine

Years since first introduction

Why Prevention Not a Priority

• Role of spina bifida and anencephaly vastly under estimated by Global Burden of Disease reports

• Role of spina bifida and anencephaly as a cause of child death and disability not appreciated by potential funders
Importance of folic acid preventable spina bifida and anencephaly not understood

• Each year 20 times as many children affected as were in all years damaged by thalidomide.
Why Can’t We Prevent as Well as the Vaccine People?
Nutrition Regulators Must Be Led to Mandatory Folic Acid Fortification

• Nutrition regulators all over the world and especially in Europe fail by not requiring folic acid fortification

• Parents and health professionals are very effective at convincing regulators to do what they should already have done.

• Prevention helps parents and professional by freeing up resources to care for those with spina bifida
Importance of spina bifida and anencephaly not understood

- Is a major cause of child mortality and not recognized by foundations giving money to prevent child death
- In India about 10% of child mortalities caused by folic acid preventable spina bifida and anencephaly
- Globally about as many affected children as there were children who had polio
- Each year 20 times as many children affected as were in all years damaged by thalidomide.
Folate Deficiency Main Cause of Spina Bifida
Epidemics

• Major clue that the primary cause was environmental rather than genetic
• Major epidemics continue today
Major limitations to global SBA F prevention

• Lack of a taskforce with the purposeful goal of total prevention of SBA F
• Researchers underestimate pregnancies affected by SBA F and the role of SBA F in child mortality
Boston and Providence
Flour fortification with folic acid has a high cost:benefit ratio for preventing spina bifida

<table>
<thead>
<tr>
<th>Ratio</th>
<th>Country</th>
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<tbody>
<tr>
<td>1:12</td>
<td>Chile</td>
</tr>
<tr>
<td>1:30</td>
<td>South Africa</td>
</tr>
<tr>
<td>1:20-1 50</td>
<td>USA</td>
</tr>
</tbody>
</table>

Good News

• 35,000 folic acid preventable spina bifida and anencephaly prevented yearly by mandatory folic acid fortification

• 350,000 children born without spina bifida or folic acid over the last 10 years

• Wonderful news for parents who are unaware of how this prevention changed their lives
NTD prevalence rates before and after fortification compared to China Community Trial of 400 mcg folic acid daily

Canada

Prevalence rates before fortification:
- 10.6
- 7.6
- 9.7
- 11.3
- 15.4
- 9.3
- 6.7
- 7.5
- 6.3
- 9.7
- 17.0
- 13.9
- 10.1
- 9.0
- 7.0
- 6.0

Prevalence rates after fortification:
- 45.6
- 27.2
- 12.6
- 17.7
- 11.2
- 9.6
- 10.0
- 48.0
<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
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<tbody>
<tr>
<td>1935</td>
<td>American epidemic of SBA—5 per 1000 births or 50 per 10,000</td>
</tr>
<tr>
<td>1991</td>
<td>Folic acid proven to prevent SBA F: UK MRC study</td>
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<tr>
<td>1991</td>
<td>USA high-risk recommendation</td>
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<tr>
<td>1992</td>
<td>USA population recommendation</td>
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<tr>
<td>1996</td>
<td>USA regulations permitted and then required by January 1, 1998, mandatory folic acid fortification of “enriched cereal grain products”</td>
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<tr>
<td>1998</td>
<td>USA successfully implementation of mandatory folic acid fortification</td>
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<tr>
<td>2014</td>
<td>Non folic-preventable spina bifida and anencephaly determined to be 0.5 per 1000 births or 5 per 10,000—90% reduction</td>
</tr>
</tbody>
</table>
Mandatory folic acid fortification in Australia

• In 2009, folic acid and iodine were included in the fortification mandate in Australia.

• In 2016, post-fortification prevalence of neural tube defects decreased by:
  - 14.4% (overall)
  - 55.0% (teenagers)
  - 74.0% (Aboriginal and Torres-Strait Islander Women)


Cases per 100 000

- Conj vax 18 mo
- Conj vax 2 mo

Adams WG, JAMA 1993
2015 Status of Global Prevention of FAP SBA

Modest and High Prevention estimated using daily folic acid consumption of 100 mcg/day (range 20-150 mcg/day) and 200 mcg/day (≥151 mcg/day), respectively, from fortified wheat or maize flour.

Source: Center for Spina Bifida Research, Emory University (Accepted for Publication – Birth Defects Res Part A)
Global Burden of Spina Bifida and Anencephaly (Year 2015)

328,000 cases of spina bifida and anencephaly worldwide annually

246,000 cases are folic acid preventable

Prevented 13% Not Prevented 87%

13% prevention in 58 countries implementing mandatory folic acid fortification (adding at least 1.0 ppm folic acid to wheat / maize flour) worldwide during the year 2015
Mandatory Folic Acid Fortification is Safe!

- Mandatory folic acid fortification adds less than the Recommended Daily Allowance (RDA) of folic acid (~140 mcg/day)
- It is perfectly safe!
WHO Blood Folate Concentration Surveillance Tools

GUIDELINE:
OPTIMAL SERUM AND RED BLOOD CELL FOLATE CONCENTRATIONS IN WOMEN OF REPRODUCTIVE AGE FOR PREVENTION OF NEURAL TUBE DEFECTS

Blood folate insufficiency, not deficiency, is the relevant measure for neural tube defect prevention.

Folate deficiency

Folate insufficiency

Crider K S et al. BMJ 2014;349:bmj.g4554
Making Spina Bifida and Anencephaly More Visible

• Provide data that accurately shows role mandatory folic acid fortification in preventing child deaths:
  – India
    • 100,000 deaths a year
    • 8 per cent of child deaths
    • Saves money, too