Advancing Preconception Care: Moving from Evidence to Implementation

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UNICEF photo from Burundi
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Main Messages
1. Neural tube defect risk can be reduced if women have optimum folate status before and in early pregnancy.
2. We can only meet global infant mortality targets by reducing birth defects
3. With all folic acid interventions, we should aim to reach a birth prevalence of ~6 neural tube defects/10,000
4. Food fortification is the best public health approach to deliver folic acid to women in the peri-conceptional period
5. You should act to ensure food fortification with folic acid is implemented & monitored in your country.
Role of Nutrition in Preconception Health

Maternal Pre-conception Nutrition Status

- **Underweight**:
  - ↑ Preterm birth
  - ↑ Small for gestational age

- **Folate insufficiency**:
  - ↑ Neural tube defects

Overweight:
- ↑ Pre-eclampsia
- ↑ Macrosomia

Maternal, Newborn & Child Health Outcomes

Dean 2014
Neural Tube Defects (NTDs)

Birth defect affecting the brain and spinal cord
Neural Tube Closes ~4 Weeks after Conception

For women to have optimum folate status by this time, must act before pregnancy

Weeks post-conception
Spina Bifida

Cyst on baby’s back from spina bifida

A. Spina bifida occulta
B. Spina bifida with meningocele
C. Spina bifida with meningo(myelo)cele
D. Spina bifida with myeloschisis

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NIH 2013
Anencephaly
~320,000 Pregnancies Affected with Neural Tube Defects Annually

Global neural tube defects birth prevalence: 24/10,000
Opportunities to Reduce Neural Tube Defects
Neural Tube Defects are Preventable with Folic Acid

72% of neural tube defects were prevented through the administration of folic acid to women
WHO Recommendations

Prevention of neural tube defects

INTEGRATED MANAGEMENT OF PREGNANCY AND CHILDBIRTH (IMPAC)

The standard

All women, from the moment they begin trying to conceive until 12 weeks of gestation, should take a folic acid supplement. Women who have had a fetus diagnosed as affected by a neural tube defect (NTD) or have given birth to a baby with NTD should receive information on the risk of recurrence, be advised on the protective effect of periconceptional folate supplementation and be offered high-dose supplementation.

Aim

To prevent NTDs and other congenital malformations in the fetus.

Requirements
WHO Recommendations

- Women trying to conceive need **400 μg folic acid daily**, starting two months before the planned pregnancy.
- Pregnant women need to continue taking **400 μg folic acid daily** until they are 12 weeks pregnant.
WHO Recommendations

- Pregnant women who have previously had a baby with a NTD, have diabetes, or who are under anticonvulsant treatment need **5 mg folic acid daily** plus increased food folate intake.

NTD, neural tube defect
Ensure healthy lives and promote well-being for all at all ages

TARGETS

3.1
By 2030, reduce the global maternal mortality ratio to less than 70 per 100,000 live births

3.2
By 2030, end preventable deaths of newborns and children under 5 years of age, with all countries aiming to reduce neonatal mortality to at least as low as 12 per 1,000 live births and under-5 mortality to at least as low as 25 per 1,000 live births

3.3
By 2030, end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases and other communicable diseases

3.4
By 2030, reduce by one third premature mortality from non-communicable diseases through prevention and treatment and promote mental health and well-being

3.5
Strengthen the prevention and treatment of substance abuse, including narcotic drug abuse and harmful use of alcohol

3.6
By 2020, halve the number of global deaths and injuries from road traffic accidents

3.7

https://sustainabledevelopment.un.org/topics
Globally: Annual Deaths Decreased in Children <5 Years

Most of the reductions were in children 1-4 years and due to decreases in infectious disease-related mortality: pneumonia, measles, diarrhea

Increase in proportion of deaths occurring in neonatal period (1-28 days)

Bhutta 2013, Black 2010
When Mortality from Infections is Lower, Burden from Birth Defects* is Higher

Infection deaths due to pneumonia (15% + 3%) + measles (1%) + diarrhea (18% + 1%) = 38%

Infection deaths due to pneumonia (11% + 3%) + measles (0%) + diarrhea (5%) = 19%

* Birth defects & congenital anomalies are used synonymously

Black 2010, Bhutta 2013, WHO 2015
Public Health Strategies to Reduce the Risk of Neural Tube Defects
Provide Vitamin B9

FOOD FOLATE

FOLIC ACID

www.breakingmuscle.com
Sources of Food Folate

WHO recommendations to prevent neural tube defects: folic acid (primarily)

Suitor 2000, WHO 2007
Sources of Folic Acid

- **Folic Acid**
  - Dietary Supplements Containing Folic Acid
  - Foods Fortified with Folic Acid
Dietary Supplements Containing Folic Acid

Women planning a pregnancy were given daily
- folic acid and other nutrients (in the vitamin group), or
- other nutrients (in the trace-element group)

Folic acid supplements given daily to women reduce the first occurrence of a neural tube defect

Table 3. Congenital Malformations, According to Study Group.

<table>
<thead>
<tr>
<th>Malformation</th>
<th>Vitamin Group</th>
<th>Trace-Element Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neural-tube defect</td>
<td>0</td>
<td>6</td>
</tr>
</tbody>
</table>

$P = 0.29$

Czeizel 1992
Folic Acid Supplement Use is Low

- Assessed in 49 studies from 22 countries
- Peri-conceptional use ranged from 0.5% (Italy) - 52% (Netherlands)

In practice, folic acid supplement use is low

Ray 2004
Many Pregnancies are Unplanned

“Almost half of all pregnancies worldwide, estimated to be over 100 million annually, are unintended or mistimed.”

If women are not planning pregnancy, they may not take supplements in peri-conceptional period.
Folic Acid Supplementation AND Fortification

• Compared NTD levels before and after recommendations were issued for folic acid supplementation (~1992)

• 13 birth defects registries; 9 European countries + Israel

• “The issuing of recommendations on folic acid [supplementation] was followed by no detectable improvement in the trends of incidence of neural tube defects.”

All women capable of becoming pregnant should be encouraged to take folic acid supplements AND...

NTD, neural tube defect
Food Fortification with Folic Acid

Fortification: the addition of nutrients to foods during processing

Without behavior change, women continue to eat foods, now fortified with folic acid. Extra folic acid will improve women’s folate status. Women with unplanned pregnancies will have optimal folate status to prevent NTDs.

NTDs, neural tube defects
84 countries require fortification of wheat flour, maize flour, and/or rice

Wheat flour: 83
Maize flour: 14
Rice: 6

August 2015. Source: Food Fortification Initiative.
To request data, e-mail info@ffinetwork.org
Global Experience of Grain Fortification with Folic Acid

• Mandate fortification with folic acid
  - Wheat flour: 79 of 84 countries
  - Maize flour: 12 of 14 countries
  - Rice: 4 of 6 countries

• Folic acid levels required
  - Wheat flour: 0.5-3.3 mg/kg
  - Maize flour: 0.5-2.5 mg/kg
  - Rice: 1-3.08 mg/kg

mg/kg = parts per million (ppm)
Grain Fortification in Africa
African Countries with Grain Fortification Mandates

Wheat flour (n=26)
- Benin
- Burkina Faso
- Burundi
- Cameroon
- Cape Verde
- Congo
- Cote d’Ivoire
- Djibouti
- Egypt
- Ghana
- Guinea
- Kenya
- Liberia
- Malawi
- Mali
- Mauritania

Maize flour (n=8)
- Burundi
- Kenya
- Malawi
- Nigeria
- Rwanda
- South Africa
- Tanzania
- Uganda

Rice (n=0)
African Experience of Grain Fortification with Folic Acid

• Mandate fortification with **folic acid**
  - Wheat flour: 24 of 26 countries (*Exceptions: Congo, Nigeria*)
  - Maize flour: 7 of 8 countries (*Exception: Nigeria*)

FFI 2015; maps from es.Wikipedia.org
Evidence for grain fortification with folic acid reducing neural tube defects
6/10,000: Lowest Birth Prevalence of NTDs with Folic Acid

Optimal population red blood cell (RBC) folate concentration to prevent neural tube defects (NTDs)

Global NTD birth prevalence: 24/10,000
Goal: All countries’ NTD birth prevalence to reach 6/10,000

Crider 2015, March of Dimes 2006
Reductions in Neural Tube Defects (NTDs) after Flour Fortification with Folic Acid was Initiated

Fortification of wheat flour ± maize flour; folic acid in flour ranged from 1.2-2.2 mg/kg

FFI 2012, updated 2015
Goal: All Countries’ NTD Birth Prevalence to Reach 6/10,000

Prefortification NTD per 10,000
Postfortification NTD per 10,000

Brazil  Canada  Chile  C Rica  Iran  Jordan  Peru  S Arabia  S Africa  USA

FFI 2012, updated 2015
Globally an estimated 38,417 birth defects were prevented in 2012 – an average of 105 a day – where flour was fortified with folic acid.
Favorable Cost:Benefit Ratio for Fortification Preventing Spina Bifida

- **Chile**: 1:12
- **South Africa**: 1:30
- **USA**: 1:48

Costa Rica Experience with Multiple Fortified Foods

Neural Tube Defects per 10,000 Live Births

- Pre-fortification (1987-1998): 9.8
- Post-fortification (2003-2012): 4.8

Depending on the food patterns in a country, one or multiple foods may need to be fortified with folic acid to have maximum benefit.

Foods fortified with folic acid: wheat flour, maize flour, dairy products, rice

Barboza 2014
Challenges in fortification with folic acid
Can have Greater Public Health Impact

~25% of FAP SBA is being prevented through flour fortification with folic acid

Dr. Vijaya Kancherla to present updated estimates in Symposia 9 (Thursday)
Increasing Price of Folic Acid

www.phillyliving.com
Concerns with Folic Acid

Fortification with folic acid does not

- Increase the incidence of cancer
- Mask vitamin B12 deficiency
- Cause dietary folic acid to exceed the Tolerable Upper Intake Level

Limited Laboratory Capacity to Analyze RBC Folate

- WHO guidelines: RBC folate to estimate NTD risk
- ~3 laboratories with capacity to conduct RBC folate analyses using gold standard measure

RBC, red blood cell; NTD, neural tube defect
What You Can Do
Your Role

- Meet with National Fortification Alliance
- Turn knowledge into action
- Organize tours
- Speak with influential people
- Request assistance

Food fortification with folic acid successfully implemented & monitored in your country
Conclusions (1)

1. Neural tube defect risk can be reduced if women have optimum folate status before and in early pregnancy
2. We can only meet global infant mortality targets by reducing birth defects
3. With folic acid interventions, we should aim to reach a birth prevalence of ~6 neural tube defects/10,000
Conclusions (2)

4. Food fortification is the best public health approach to deliver folic acid to women in the peri-conceptional period

5. You should act to ensure food fortification with folic acid is implemented & monitored in your country
For More Information

Smarter Futures  www.smarterfutures.net/

Food Fortification Initiative (FFI)  www.FFInetwork.org

International Federation For Spina Bifida and Hydrocephalus  http://www.ifglobal.org/en/

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