# Could folic acid supplementaion bridge the gap of the results of fortification?

State of the art in Europe and future prospectives

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# The Continuum of Reproductive Health

- Improving health of infants requires focusing on the entire spectrum of reproductive health which extends from prior to conception through the first year of an infant's life and throughout the woman's childbearing years
- Folic acid supplementation is a key preconception factor in preventing neural tube defects



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Prevention of Neural Tube Defects by Periconceptional Folic Acid Supplementation in Europe

December 2005

### **Special Report 2005**

- Reccomandations 0.4 mg in 11/18 countriesi
- 1992-1993 GB, Ireland, Holland
- Italy 2004

"The situation regarding low uptake of supplementation is reflected in the lack of a clear decline in the prevalence of neural tube defects across Europe"

### 2004 Folic acid Network Italy

- Reccomandations 0.4 mg
- Inclusion of all stakeholders: academics, patient groups, ministry of health, pharmaceutical companies, congenital anomaly registries

# Most Pregnancies Are Unplanned!

- About half of all pregnancies are unplanned
- Unplanned pregnancies are most common among teens
- Depending on the age of the woman, the percentage of unplanned pregnancies varies from 33% – 78%

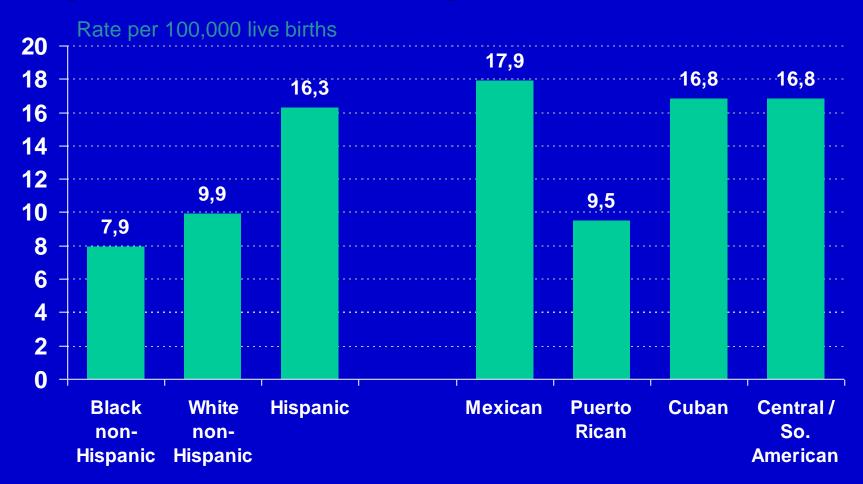
## **Epidemiology of NTD's**

 Occur in about 2 per 1000 births across Europe

 Most babies with NTD's are born to women with no risk factors

 Racial/ethnic variation in incidence of NTD's

# Infant Deaths due to NTDs by Race/Ethnicity, United States



Source: National Center for Health Statistics, 1996 period linked birth/infant death file Prepared by March of Dimes Perinatal Data Center, 1999

# Three Approaches for Changing Behavior



# Should Europe fortify a staple food with folic acid?

\*Lenore Abramsky, Helen Dolk, on behalf of the EUROCAT Folic Acid Working Group

The Lancet 369 Feb 2007



# Should Europe fortify a staple food with folic acid?

 "The main obstacle has been the concern that the known benefit of folic acid to the few (women who become pregnant) and the potential benefits to the many (for example, the possible prevention of cardiovascular disease) might be outweighed by some yet unknown risk for the general population"

#### **Evaluation of risks and benefits**

 The studies that support the benefits of folic acid are constantly increasing

Studies that suggest the need for caution have emerged

#### Reduction in Orofacial Clefts Following Folic Acid Fortification of the U.S. Grain Supply

Mahsa M. Yazdy,1,2 Margaret A. Honein,1 and Jian Xing1

<sup>1</sup>National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, Georgia
<sup>2</sup>Oak Ridge Institute for Science and Education, Oak Ridge, Tennessee

Received 30 June 2006; Revised 6 September 2006; Accepted 12 September 2006

#### Yazdy et al Sett 2006

• "Folic acid fortification in the United States was associated with a small decrease in orofacial cleft palate prevalence, with the timing of the decline consistent with the introduction of fortification"

1: Cancer Epidemiol Biomarkers Prev. 2007 Jul; 16(7): 1325-9.

A temporal association between folic acid fortification and an increase in colorectal cancer rates may be illuminating important biological principles: a hypothesis.

#### Mason JB, Dickstein A, Jacques PF, Haggarty P, Selhub J, Dallal G, Rosenberg IH.

Jean Mayer U.S. Department of Agriculture Human Nutrition Research Center on Aging at Tufts University, Boston, MA 02111, USA. joel.mason@tufts.edu

Nationwide fortification of enriched uncooked cereal grains with folic acid began in the United States and Canada in 1996 and 1997, respectively, and became mandatory in 1998. The rationale was to reduce the number of births complicated by neural tube defects. Concurrently, the United States and Canada experienced abrupt reversals of the downward trend in colorectal cancer (CRC) incidence that the two countries had enjoyed in the preceding decade: absolute rates of CRC began to increase in 1996 (United States) and 1998 (Canada), peaked in 1998 (United States) and 2000 (Canada), and have continued to exceed the pre-1996/1997 trends by 4 to 6 additional cases per 100,000 individuals. In each country, the increase in CRC incidence from the prefortification trend falls significantly outside of the downward linear fit based on nonparametric 95% confidence intervals. The statistically significant increase in rates is also evident when the data for each country are analyzed separately for men and women. Changes in the rate of colorectal endoscopic procedures do not seem to account for this increase in CRC incidence. These observations alone do not prove causality but are consistent with the known effects of folate on existing neoplasms, as shown in both preclinical and clinical studies. We therefore hypothesize that the institution of folic acid fortification may have been wholly or partly responsible for the observed increase in CRC rates in the mid-1990s. Further work is needed to definitively establish the nature of this relationship. In the meantime, deliberations about the institution or enhancement of fortification programs should be undertaken with these considerations in mind.

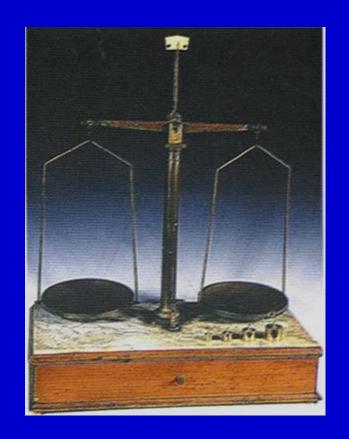
PMID: 17626997 [PubMed - indexed for MEDLINE]

#### Mason et al July 2007

• "we therefore hypothesize that the institution of folic acid fortification may have been wholly or partly responsible for the observed increase in CRC rates in the mid-1990's"

#### **Evaluation of risks and benefits**

 Use our knowledge to clarify and update reccomendations and engage decision makers in public health policy



### PRIMARY PREVENTION OF CONGENITAL ANOMALIES

EUROCAT (European Surveillance of Congenital Anomalies) and EUROPLAN (European Project for Rare Diseases National Plans Development)

Recommendations on policies to be considered for the primary prevention of congenital anomalies in National Plans and Strategies on Rare Diseases







Grant N.: 2010 22 04

www.eurocat-network.eu

Grant N.: 2011 22 01

www.europlanproject.eu

### Supplementation Strategy

- Medical Education the right dose, the right time
- Maternal lifestyle
- All women of childbearing age
- Folic acid free of charge



This baby was born healthy.

