



## Can the Rate of Neural Tube Defects Be Further Reduced in South Carolina?

Some authorities consider that an irreducible rate of neural tube defects is approaching or has been reached in areas with folic-acid fortified cereal grain products. We consider that assumption to be

simply wrong. Dean *et al.* report in the November issue of the *Journal of Pediatrics* (226:186,2020) that isolated NTDs in South Carolina continue to occur at a rate of about 25 cases per year some 20 years after fortification of cereal grain flours with folic acid. Failure to consider additional measures is tacit approval that 25 NTD cases in South Carolina and 2000 cases nationwide is acceptable.

One possibility is that post-fortification does not provide sufficient folic acid for women of childbearing years in a high risk area like South Carolina. The unanswered question is whether the rate of NTDs could be further reduced by increasing the folic acid dose in the periconceptional period to 4 mg/day.

This we propose to address with the recommendation that appears below.

## Increasing Folic Acid Intake to 4 mg/day in the Periconceptional Period

### Pros and Cons

Although 4 mg/day folic acid was used in the Medical Research Council's neural tube defects recurrence study without reported adverse effects and is currently the Center of Disease Control and Prevention's recommendation for recurrence prevention, increasing the daily dose of folic acid for all women of childbearing age must be weighed against potential side effects.

Patel and Sobczyńska-Malefora have enumerated the potential effects that might occur in certain populations, including diarrhea, rashes, sleep disturbances, masking of vitamin B12 deficiency-related neurologic damage, insulin resistance, increase in cancer risk or promotion of the growth of pre-existing cancers, and lowering the effectiveness of anticonvulsant medications. (*Eur J Clin Nutr* 71:159,2017) Other concerns relate to potential effects on the fetus, the most plausible being alteration of the methylation profile.

In contrast, Wald *et al.* have suggested that the risks are overstated and that the concept of a tolerable upper intake level of folic acid should be abandoned. (*Public Health Rec* 39:2,2018)

### Our Recommendation

The Neural Tube Defect Prevention Program at the Greenwood Genetic Center proposes that ***the standard preventive dose of folic acid for all women of childbearing age be increased to 4 mg/day during the 3 months prior to conception and the first month after conception.***

South Carolina is a high-risk state for these defects, and 4 mg/day is currently the dose recommended by the CDC for high risk pregnancies (those with a prior affected infant). Currently, women on a typical diet receive approximately 100-150 micrograms/day of folic acid through fortification of cereal grain flours. Therefore, the recommendation to use 4 mg/day of folic acid remains the same whether or not the woman uses folic acid fortified food products.

This increased dose should be used with two caveats.

(1) The folic acid should be prescribed as folic acid alone rather than by increasing the number of multivitamins, as the dose of other vitamins may become excessive. This increased dose of folic acid may be used in addition to a single multivitamin with 0.4 mg folic acid.

(2) If any of the potential side effects enumerated above should occur, discontinue the 4 mg/day dose and return to the multivitamin with only 0.4 mg/day or prenatal vitamin with 0.8 mg/day alone.

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### Neural Tube Defects and Associated Anomalies before and after Folic Acid Fortification

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**Objective** To examine the prevalence and types of neural tube defects and the types of anomalies co-occurring with neural tube defects in 6 years before fortification of cereal grain flour with folic acid (1992-1998) and 20 years after fortification (1999-2018) in South Carolina, a state with a historically high prevalence of these birth defects. **Study design** The prevalence of neural tube defects was determined by active and passive surveillance methods in South Carolina since 1992. The types of neural tube defects and co-occurring malformations were determined by prenatal ultrasound and post-delivery examination.

**Results** In the 6 prefortification years, 363 neural tube defects were identified among 279 163 live births and fetal deaths (1/769), 305 (84%) of which were isolated defects of the calvaria or spine. In the 20 fortification years, there were significant reductions in the prevalence and percentage of isolated defects: 938 neural tube defects were identified among 1 165 134 live births and fetal deaths (1/1242), 696 (74.2%) of which were isolated. The current prevalence of neural tube defects in South Carolina (0.56/1000 live births and fetal deaths) is comparable with that nationwide.


**Conclusions** The continued occurrence of neural tube defects, the majority of which are isolated, after folic acid fortification of cereal grain flours suggests that additional prevention measures are necessary to reduce further the prevalence of these serious defects of the brain and spine. (J Pediatr 226:186, 2020)

## Greenwood Genetic Center

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### Governor Declares January 2021 Birth Defects Awareness Month

January 2021 has been designated by SC Governor Henry McMaster as Birth Defects Awareness Month. As part of Birth Defects Awareness Month, billboards have been placed throughout South Carolina in efforts to increase awareness about the importance of taking a multivitamin containing folic acid to prevent birth defects of the brain and spine. The message will be continued during the subsequent months through public lectures, science courses, press releases and exhibits.



**Fabulous Folate**  
Oh Baby, It's Good for YOU!

SC Department of Disabilities & Special Needs • SC Department of Health & Environmental Control  
Greenwood Genetic Center

**A daily multivitamin with folic acid improves your health now – prevents birth defects later.**

**1-800-6-SOMEDAY**

### NTDs in SC during 2020 (Project year 28)

The number of NTDs reported during 2020 (Year 28) declined significantly. Because this occurred during year 1 of the COVID pandemic, there is concern that all cases may have not been accounted for due to improper coding or some other issue. We will be verifying through Vital Records that all NTDs in South Carolina have been identified by the surveillance system.

#### Cases by type of NTD:

According to current data for 2020, spina bifida was more common than anencephaly, accounting for 50% of cases.

<b>Spina bifida</b>	<b>10 (50%)</b>
<b>Anencephaly</b>	<b>8 (40%)</b>
<b>Encephalocele</b>	<b>2 (10%)</b>

#### Detection method:

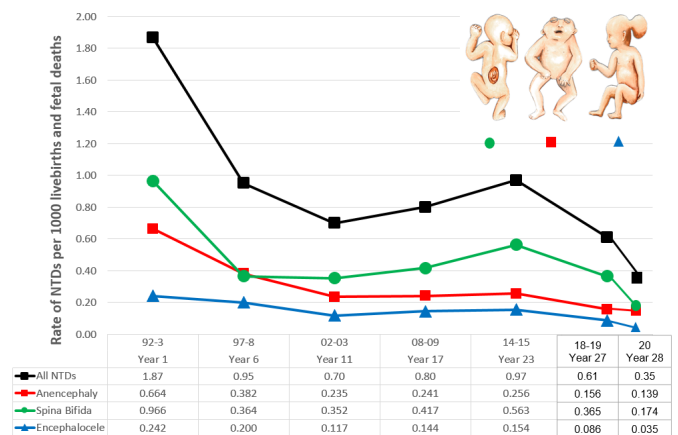
The majority of NTDs were detected by ultrasound during the early part of pregnancy. One was not detected until delivery.

<b>Ultrasound</b>	<b>17</b>
<b>Quad screen</b>	<b>2</b>
<b>Delivery</b>	<b>1</b>

#### Distribution of cases by geographic region for year 28:

<b>Region I (Piedmont)</b>	<b>11</b>
<b>Region II (Midlands)</b>	<b>5</b>
<b>Region III (Coastal)</b>	<b>4</b>

### Neural Tube Defects in South Carolina 1992-2020



#### Contact Us:

Staff members at the office of the South Carolina Birth Defects Prevention Program will be happy to assist your office in any way to assure that your patients have information regarding prevention of these serious defects. We now have literature on NTDs and NTD prevention available in Spanish. A dietary guideline with foods that are high in folic acid along with examples of menus using this information has proven to be a very helpful tool with the Hispanic communities.

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