

Neural Tube Defects (NTD): Folic Acid and Pregnancy ^[1]

By: Cooper-Roth, Tristan Keywords: Congenital disorders ^[2] Human development ^[3]

In the US, one in 1000 births is affected by [neural tube](#) ^[4] defects (NTD). A [neural tube](#) ^[4] defect is a birth defect involving the malformation of body features associated with the brain and spinal cord. An NTD originates from and is characterized by incomplete closure of the [neural tube](#) ^[4], which is an [organizer](#) ^[5] and precursor of the [central nervous system](#) ^[6]. In [humans](#) ^[7], incomplete closure of the [neural tube](#) ^[4] during embryonic development results in anatomical abnormalities such as anencephaly (a lack of skull and brain), hydranencephaly (cerebral hemispheres replaced with sacs of cerebrospinal fluid), [spina bifida](#) ^[8] occulta (incompletely closed lower spinal cord), iniencephaly (severe retroflexed head and spinal defects), and encephalocele (a sac-like protrusion from an opening somewhere along the midline of the skull).

NTDs originate very early in development, in [humans](#) ^[7] typically during the fourth week after [conception](#) ^[9], a particularly vulnerable period. The causes of NTDs are not well understood, but are thought to be complex, involving one or more of a variety of genetic, environmental, and nutritional factors. One of the most important findings is that a deficiency of vitamin B9 (folate or [folic acid](#) ^[10]) in the mother's diet greatly increases the chances that her baby will have an NTD. Therefore, the importance of the mother consuming essential vitamins both before and during [pregnancy](#) ^[11] is emphasized for the wellbeing of a developing embryo.

The word folate comes from the Latin folium, meaning "a leaf." Folate is found primarily in green-leafed vegetables, legumes, liver, and certain seeds. Folic acid, its more stable synthetic equivalent, is used to fortify grain products such as flour and is converted into a metabolically active form in the liver. Folate derivatives hold the unique capacity of conducting one-carbon transfers, which is necessary in methylation reactions and nucleic acid synthesis.

Methylation reactions and nucleic acid synthesis aid in the biosynthesis of both DNA and RNA. A deficiency in [folic acid](#) ^[10], or a lack of the proper enzymes to metabolize [folic acid](#) ^[10] into folate, sets the stage for NTDs because of failure to biosynthesize the proper nucleotides during early pregnancy—a crucial time when the embryo exhibits rapid cell division and cell growth, requiring DNA synthesis to be at its utmost efficiency. With the embryo lacking the ability to biosynthesize DNA at an efficient rate, and thus to form the necessary proteins, the [neural tube](#) ^[4] does not close correctly.

Because of the growing understanding of what causes NTDs, the US Department of Human Health Services issued a recommendation in 1992, endorsed by the American Academy of Family Physicians and the American College of Obstetrics and Gynecology, for all sexually active women who are capable of becoming pregnant to consume a daily dosage of 0.4 mg of [folic acid](#) ^[10]. The potential of folate as a preventative medicine was then recognized by the [Food and Drug Administration](#) ^[12] (FDA) in 1996. The FDA soon thereafter administered a [regulation](#) ^[13] to all cereal-grain companies requiring them to fortify their products with [folic acid](#) ^[10] using a concentration of 140 µg/100 g. With this dietary regime, it has been estimated that

50% of all human NTDs can be avoided.

Sources

1. Gilbert, Scott F. *Developmental Biology* ^[14], 8th ed. Sunderland, MA: Sinauer Associates, 2006, 379-80.
2. U.S. Preventive Services Task Force. *Folic Acid for the Prevention of Neural Tube Defects: U.S. Preventive Services Task Force Recommendation Statement*. AHRQ Publication No. 09-05132-EF-2, May 2009. Agency for Healthcare Research and Quality, Rockville, MD. <http://www.ahrq.gov/clinic/uspstf09/folicacid/folicacidrs.htm> ^[15] (Accessed February 10, 2010).
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Publisher

Arizona State University. School of Life Sciences. Center for Biology and Society. Embryo Project Encyclopedia.

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Format

Articles ^[20]

Last Modified

Wednesday, July 4, 2018 - 04:40

DC Date Accessioned

Friday, May 25, 2012 - 15:47

DC Date Available

Friday, May 25, 2012 - 15:47

DC Date Created

2010-10-20

DC Date Created Standard

Wednesday, October 20, 2010 - 07:00

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Arizona 85287, United States

Source URL: <https://embryo.asu.edu/pages/neural-tube-defects-ntd-folic-acid-and-pregnancy>

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