



Infant Nutrition Council

Industry supporting both Breastfeeding & Infant Formula

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Vitamins and congenital malformations

Studies have shown that the B vitamin folic acid (folate) is involved in the development of the fetal brain and spinal cord and that malformations of those areas, in the form of spina bifida and less often, anencephaly can sometimes be due to low levels of the vitamin in the mother. This discovery has come after over 40 years' study in the use of folate supplements in pregnancy and the proposal to add the vitamin to bread. It is clear that the problem is a combination of low population intake of the vitamin, and a genetic variant of a key enzyme necessary for its activation which makes the enzyme less efficient.

The story and the success of supplementation in reducing the frequency of the condition in many countries has diverted attention from possible relationships between folate or other vitamins, and other congenital malformations.

Folate and Hydrocephalus

Although there is evidence that low folate levels may be associated with other congenital malformations as well, such as congenital heart malformations, we have had almost no experimental confirmation of this.

A UK study, albeit in rats, has found that in a strain of rat prone to the serious malformation Hydrocephalus, administration of folate derivatives can reduce the risk to the fetus. Hydrocephalus is a condition in which there is a developmental blockage to the flow of cerebrospinal fluid which results in a rising pressure within the brain, marked head enlargement and brain damage.

Curiously although administration of folic acid to the mothers actually *increased* the risk of hydrocephalus, administering two related molecules, tetrahydrofolic acid and 5formyltetrahydrofolic acid, substantially reduced the risk. It was further shown that these animals have a genetic defect in one of the three enzymes in the cerebrospinal fluid which metabolise folate.

Whether this has any relevance to the human condition is another matter entirely, but as hydrocephalus is a treatable but troublesome condition, further investigation is warranted.

Cains S, Shepherd A, Nabiuni M, Owen-Lynch PJ, Miyan J: Addressing a Folate Imbalance in Fetal Cerebrospinal Fluid Can Decrease the Incidence of Congenital Hydrocephalus. *J Neuropathol Exp Neurol*. 2009 Mar 12. [Epub ahead of print].

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