

1). Associations between lower serum folate or cobalamin levels and higher homocysteine levels and the development of decreased cognitive function and dementia in Alzheimer's disease have been reported. A meta-analysis of randomized, placebo-controlled trials of homocysteine-lowering B-vitamin supplementation of individuals with and without cognitive impairment, however, showed that supplementation with vitamin B₁₂, vitamin B₆, and folic acid alone or in combination did not improve cognitive function. Some studies done in China suggest some cognitive improvement with supplements of both vitamins. It is unknown whether prolonged treatment with these B vitamins can reduce the risk of dementia in later life.

■ GENERAL TISSUE EFFECTS OF COBALAMIN AND FOLATE DEFICIENCIES

Epithelial Surfaces After the marrow, the next most frequently affected tissues are the epithelial cell surfaces of the mouth (with glossitis), stomach, and small intestine and the respiratory, urinary, and female genital tracts. The cells show macrocytosis, with increased numbers of multinucleate and dying cells. The deficiencies may cause cervical smear abnormalities.

Complications of Pregnancy The gonads are also affected, and infertility is common in both men and women with severe deficiency of either vitamin. Maternal folate deficiency has been implicated as a cause of prematurity, and both folate deficiency and cobalamin deficiency have been implicated in recurrent fetal loss and neural tube defects, as discussed below.

Neural Tube Defects Folic acid supplements at the time of conception and in the first 12 weeks of pregnancy reduce by ~70% the incidence of neural tube defects (NTDs) (anencephaly, meningomyelocele, encephalocele, and spina bifida) in the fetus. Most of this protective effect can be achieved by taking folic acid, 0.4 mg daily, at the time of conception.

The incidence of cleft palate and harelip also can be reduced by prophylactic folic acid. There is no clear simple relationship between