
What is optimal folate status?

FROM THE LABORATORY

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Folate is essential for DNA synthesis and cell growth. Deficiency is particularly harmful in pregnancy and is associated with an increased risk of foetal malformations.

High concentrations of folate are present in vegetables and fruit, but the vitamin is unstable, and 50–80 % is lost in cooking. In the United States and some other countries, breakfast cereals and flour are fortified with synthetic folate, folic acid, which is reflected in the population's folate status. Median serum folate levels in American women of childbearing age are 39.0 nmol/l (1). Corresponding levels in Norwegian women in the same age group are 13.8 nmol/l (own data).

Folate requirements increase during periods of growth, pregnancy and breastfeeding. Maternal folate deficiency is associated with an increased risk of fetal malformations, and women are recommended to take 400 µg folate daily from one month before conception until the end of the first trimester to reduce

the risk of fetal neural tube defects. In countries where folic acid fortification has been introduced, the incidence of neural tube defects has fallen (2). This reduction has not been observed in Europe (3). There has been debate about whether folic acid fortification may increase the risk of cancer, but no change in the prevalence of cancer has been found in countries that have introduced this (4).

Additional intake of folate is often required throughout pregnancy and the breastfeeding period to prevent maternal deficiency (5). Folate levels in breastmilk remain high throughout the breastfeeding period, and serum folate levels are high in the first and second year of life. Folate deficiency is rare in young children (6).

It is sufficient to measure serum folate when investigating folate status. Serum levels are rapidly affected by changes in intake or absorption, which makes serum folate well-suited as a marker of nutritional status and intestinal function.

Along with cobalamin, folate is needed to remethylate homocysteine to methionine, and a deficiency in either of these two vitamins will increase homocysteine levels and reduce methionine levels. In older children and adults, homocysteine levels are primarily a folate marker, and they start to rise when serum folate levels fall below 25–27 nmol/l (Figure 1), as an indication of sub-optimal intracellular folate status. A daily intake of 300–400 µg folate in adults is associated with stable plasma homocysteine levels.

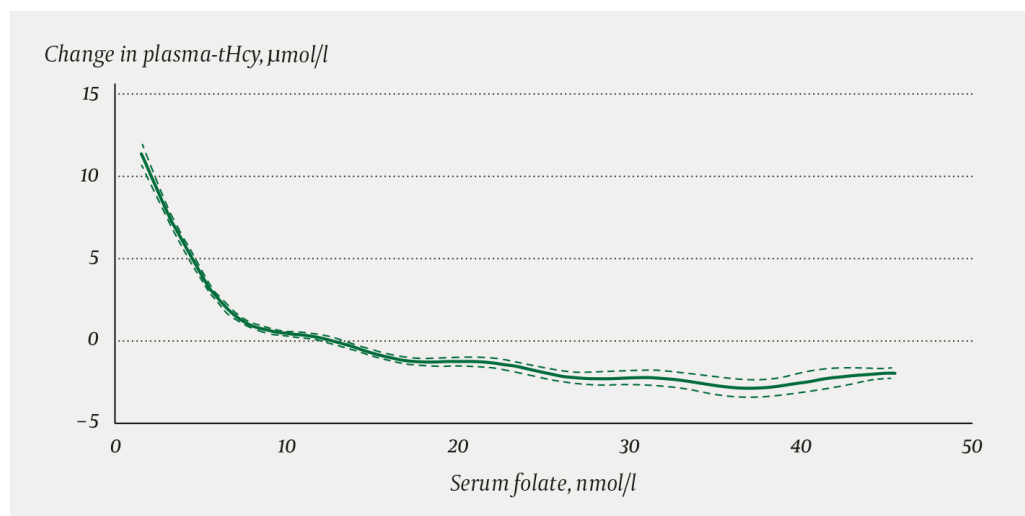


Figure 1 Change in total homocysteine levels (tHcy) in plasma in relation to serum folate in adults aged over 16 years with glomerular filtration rate (GFR) > 60 ml/min/1.73 m². The values on the y-axis indicate change from the mean tHcy. The dotted lines show the 95 % confidence interval. The figure is based on patient data (n = 12,988) from the Department of Medical Biochemistry and Pharmacology at Haukeland University Hospital.

In cases of severe folate deficiency, plasma homocysteine levels can increase to as much as 40–50 µmol/l. Individuals homozygous for the C677T polymorphism in the *MTHFR* gene (methylenetetrahydrofolate reductase) (prevalence 5–15 %), may develop higher homocysteine levels (up to 100 µmol/l) at low serum folate values, and serum folate levels > 15 nmol/l are advised in these patients (7).

The World Health Organization recommends a cut-off value for folate deficiency of <10 nmol/l (8). In women of childbearing age, serum folate levels should be > 25.5 nmol/l to prevent fetal malformations (9). This corresponds to the level of red blood cell folate that has been demonstrated in studies to provide increased genomic stability (10) and stable low plasma homocysteine levels in adults (Figure 1).

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