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Is dietary intake of folate too low?

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In today's *Lancet*, Jane Durga and colleagues[1] report a favourable effect of folic acid supplementation on cognitive decline in adults aged 50–70 years. By design, the trial was focused on people whose folate status was inadequate, as shown by a raised homocysteine concentration in the absence of other disorders or diseases that could account for the raised concentration (eg, vitamin B12 deficiency, renal disease). The trial was well designed and unique in its approach of targeting individuals who might benefit from folate supplementation. But how well do the folate intakes of these highly selected trial participants correspond to intakes in more representative samples of the population? And, why might folate intake be so low in human populations?

Dietary intakes of folate in the trial participants were far lower than the US recommended dietary allowance (RDA) of 400 μg a day,[2] and also lower than the RDA for the Netherlands (300 μg a day), but are in line with the recommended amount of 200 μg a day in Japan and Australia. Even though the participants had low dietary intakes of folate, most did not have subnormal serum folate or erythrocyte concentrations. This fact implies that the participants were not even in the first stage of negative nutrient balance,[3] although current criteria for determining inadequate folate status are crude.[4] Raised baseline concentrations of homocysteine, together with substantial improvement in biochemical measures of folate and homocysteine and in cognitive function after folic acid treatment, suggest that previous dietary intakes might have been inadequate.

The RDA defines an intake that is sufficient to meet daily nutrient requirements of most individuals (97·5%) of the same age group. These levels are approximate, especially for folate, because 150 different forms of folate exist, and chemical analysis of their composition in food has variable accuracy. Additionally, folate is highly susceptible to oxidative destruction. 50–95% of folate content in food is estimated to be lost in storage, preparation, or manufacturing processes.[5]

Taking into consideration the many problems with accurate measurement of folate intake, population comparisons suggest that intakes vary greatly according to differences in dietary behaviours across different regions, ethnic groups, age, and socioeconomic circumstances. The richest natural food sources of folate include yeast, organ meats (eg, liver, kidney, tongue), green leafy vegetables (eg, spinach, collard greens), legumes, beans, and some fruits. The highest reported intakes of folate occur in populations with the highest consumption of vegetables, such as in countries in which the diet is similar to the Mediterranean diet.[6] For example, the mean intake of dietary folate was 559 μg a day in Greece in people who followed the traditional Cretan diet.[7] Intakes in the southern regions of Europe (France, Spain, and Portugal) are about 300–400 μg a day, and 200 μg a day in northern European regions (Ireland and Sweden).[6] Intakes are also high in countries that

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fortify grain with folic acid, such as the USA and Canada. Before fortifi cation of grain was introduced, the mean folate intake in the USA was estimated to be 275 μg a day, and 26% of the population had inadequate folate status according to serum concentrations.[8] After the introduction of fortifi cation, fewer than 1% of the US population had an inadequate serum folate status.[9] In a US study of elderly people, before the introduction of folic acid fortifi cation, homocysteine concentrations were raised in individuals with folate intakes of up to 280 μg a day.

As indicated above, many individuals within populations have folate intakes that might be suboptimum for physiological function.[10] Our knowledge about the physiological importance of homocysteine is limited, as is our defi nition of inadequate folate status. To make more informed dietary recommendations for optimum folate intake, we need randomised trials that take the approach of the FACIT trial.[1] In particular, future trials should specify inclusion and exclusion criteria that target individuals at various stages of nutrient balance. They should also include comprehensive monitoring of biochemical concentrations of folate and folate metabolites in addition to monitoring of system function, such as cognitive function.

References

1. Durga J, van Boxtel MPJ, Schouten EG, et al. Effect of 3-year folic acid supplementation on cognitive function in older adults in the FACIT trial: a randomised, double blind, controlled trial. Lancet. 2007; 369:208–16. [PubMed: 17240287]
2. Food and Nutrition Board Institute of Medicine. Dietary reference intakes for thiamin, ribofl avin, niacin, vitamin B6, folate, vitamin B12, pantothenic acid, biotin, and choline, 1998: Dietary reference intakes. Washington, DC: National Academies Press; 1998.
3. Herbert, V.; Das, KC. Folic acid and vitamin B12. In: Shils, M.; Olson, JA.; Shike, M., editors. Modern nutrition in health and disease. Philadelphia: Lea and Febiger; 1994. p. 402-25.
4. Ulrich CM, Potter JD. Folate supplementation: too much of a good thing? Cancer Epidemiol Biomarkers Prev. 2006; 15:189–93. [PubMed: 16492904]
5. Sauberlich, HE. Folate (folic acid, pterolymonoglutamic acid, folacin): Laboratory tests for the assessment of nutritional status. Boca Raton: CRC Press; 1999. p. 103-33.
6. de Bree A, van Dusseldorp M, Brouwer IA, van het Hof KH, Steegers-Theunissen RP. Folate intake in Europe: recommended, actual and desired intake. Eur J Clin Nutr. 1997; 51:643–60. [PubMed: 9347284]
7. Kafatos A, Verhagen H, Moschandreas J, Apostolaki I, Van Westerop JJ. Mediterranean diet of Crete: foods and nutrient content. J Am Diet Assoc. 2000; 100:1487–93. [PubMed: 11138441]
8. Dietrich M, Brown CJ, Block G. The effect of folate fortifi cation of cereal-grain products on blood folate status, dietary folate intake, and dietary folate sources among adult non-supplement users in the United States. J Am Coll Nutr. 2005; 24:266–74. [PubMed: 16093404]
9. Pfeiffer CM, Caudill SP, Gunter EW, Osterloh J, Sampson EJ. Biochemical indicators of B vitamin status in the US population after folic acid fortifi cation: results from the National Health and Nutrition Examination Survey 1999–2000. Am J Clin Nutr. 2005; 82:442–50. [PubMed: 16087991]
10. Selhub J, Jacques PF, Wilson PW, Rush D, Rosenberg IH. Vitamin status and intake as primary determinants of homocysteinemia in an elderly population. JAMA. 1993; 270:2693–98. [PubMed: 8133587]