Executive summary

Health Council of the Netherlands. Dietary reference intakes: vitamin B_6, folate and vitamin B_{12}. The Hague: Health Council of the Netherlands, 2003; publication no. 2003/04.

In 1992, the former Food and Nutrition Council of the Netherlands published dietary reference intakes. These recommendations for the intake of nutrients were primarily aimed at the prevention of clinical symptoms and biochemical signs of deficiencies. In recent years, increasing numbers of studies have shown that certain nutrients can also help to prevent chronic diseases. Partly as a result of this, the Health Council decided to review the dietary reference intakes. The Committee on Dietary Reference Intakes, which is charged with this task, sets out its findings in a series of recommendations. The first report, containing the dietary reference intakes for calcium, vitamin D, thiamine, riboflavin, niacin, pantothenic acid and biotin, was published in July 2000.* A year later, the second report was published, with the dietary reference intakes for energy, proteins, fats and digestible carbohydrates. The present report contains the dietary reference intakes for vitamin B_6, folate and vitamin B_{12}.

The term ‘dietary reference intakes’ is a collective term for the ‘estimated average requirement’, ‘recommended dietary allowance’, ‘adequate intake’ and ‘tolerable upper intake level’. The recommended dietary allowance and adequate intake are similar terms: they both reflect the intake level at which no signs of deficiency are observed and the risk of chronic diseases (if influenced by the nutrient concerned) is kept as small as possible. The Committee preferably determines the recommended dietary allowance, defined as the estimated average requirement plus twice the standard deviation of the requirement. It can also be calculated by multiplying the estimated average requirement

* The reports of the Health Council of the Netherlands are available at www.gr.nl.

by the result of one plus 0,02 times the coefficient of variation of the requirement. If the available data are not sufficient to determine the estimated average requirement, the Committee determines the adequate intake instead of the recommended dietary allowance. Given a requirement with a normal distribution, the estimated average requirement is the level of intake that is adequate for half of the population. Finally, the Committee specifies the tolerable upper intake level. This is the level of intake above which there is a chance that adverse effects will occur.

The dietary reference intakes are intended for use by the healthy section of the population. The Committee gives separate values for infants, young children, adolescents, adults and the elderly. In many cases, the Committee makes distinctions on the basis of gender. It also establishes dietary reference intakes for pregnant women and for women who are breastfeeding infants. The three tables in this summary contain all of the dietary reference intakes that have been derived in this report. In this executive summary, the major changes relative to the previous Dutch dietary reference intakes are discussed, as are the differences with dietary reference intakes in use in foreign countries.

Vitamin B_6

The biologically active form of vitamin B_6, pyridoxal-5-phosphate, plays a role in various processes in the body, including amino acid metabolism. Reduced intake of vitamin B_6 may increase the likelihood of coronary heart diseases, but the Committee believes that this relationship has not been convincingly scientifically proved.

The bioavailability of vitamin B_6 from food — both the naturally present vitamin B_6 and the vitamin B_6 that is added to enriched foods — is estimated to be 75% of the bioavailability of vitamin B_6 from a supplement. On the basis of this, all the amounts were converted to the amount of vitamin B_6 in the food when dietary reference intakes were determined.

Because of its role in amino acid metabolism, the vitamin B_6 requirement is also determined by protein intake. According to the Committee, this association is not linear. The Committee believes that the recommended dietary allowances that have been derived in this advisory report apply for a daily protein intake of up to 150 grams. In the case of higher consumption, 0.01-0.02 milligram's of extra vitamin B_6 should be taken for each extra gram of protein.

According to the Committee, the concentration of pyridoxal-5-phosphate in plasma is the most suitable parameter for determining the vitamin B_6 status. When there is a lack of research results of this kind, the Committee also bases the derived estimated average requirement on research that uses other status parameters, such as the

tryptophan load test and the activity coefficient of aspartate amino transferase in red blood cells.

It was possible to derive the estimated average vitamin B_6 requirement and therefore also recommended dietary allowance for four groups (the age groups from 19 up to and including the age of 50, from age 51, pregnant women and lactating women). The adequate intake has been determined for all other groups. The estimated average requirement for adults was determined on the basis of the aforementioned biochemical parameters of the vitamin B_6 status. The Committee assumed that the requirement has a coefficient of variation of 20% when calculating the recommended dietary allowance. The adequate intake of vitamin B_6 for babies up to six months old was based on the average intake of infants who are exclusively fed with human milk. The adequate intakes for children and adolescents were calculated by interpolation of the values for infants and those for adults from 19 up to and including the age of 50. The extra need for vitamin B_6 during pregnancy is based on the amount deposited in the foetus and placenta; the extra requirement of lactating women is based on the average amount secreted via breast milk by mothers who exclusively breastfeed their infant.

The new Dutch values for adult males correspond well with those in Scandinavia, in Germany, Switzerland and Austria, and in the European Union; however, these reports state lower recommended dietary allowances for women, in connection with lower protein consumption. The adjustment for women was not made in the present advisory report because of the Committee's assumption that protein intake at levels up to 150 grams per day does not affect the vitamin B_6 requirement. Dietary reference intakes

Table S1 Dietary reference intakes for vitamin B_6 in food[a], in milligrams per day.

(age) group	estimated average requirement		recommended dietary allowance		adequate intake	tolerable upper intake level
	man	woman	man	woman		
0 to 5 months	-	-	-	-	0.12[b]/0.20[c]	2
6 to 11 months	-	-	-	-	0.2	3
1 to 3 years	-	-	-	-	0.4	5
4 to 8 years	-	-	-	-	0.7	8.5
9 to 13 years	-	-	-	-	1.1	15
14 to 18 years	-	-	-	-	1.5	23
19 to 50 years	1.1	1.1	1.5	1.5	-	25
$\geq$ 51 years	1.3	1.1	1.8	1.5	-	25
pregnant women	-	1.35	-	1.9	-	25
lactating women	-	1.35	-	1.9	-	25

[a] both the naturally present vitamin B_6 and the vitamin B_6 that is added to enriched foods

[b] in the case of only breastfeeding: 0.12 mg/d

[c] in the case of formula feeding (in connection with the higher protein content): 0.20 mg/d

for vitamin B_6 in Great Britain are linked to protein consumption; the recommended dietary allowances correspond with the new Dutch values if daily protein intake is 100 grams. Owing to the use of a higher coefficient of variation of the requirement, the recommended dietary allowances for adults are a little higher than the values determined for the United States.

For the derivation of the tolerable upper intake level, the Committee subscribed to the conclusions of the European Union's Scientific Committee for Food. The upper limit is considerably lower than the value determined for the United States. The tolerable upper intake level was adjusted on the basis of body weight for the younger age groups.

Folate

The biologically active forms of folate play a major role as a co-enzyme in amino acid metabolism and in the synthesis of DNA and RNA. The folate requirement is therefore relatively high during growth and pregnancy, and deficiencies first manifest in tissues with a high division rate.

Folate that occurs naturally in foods differs chemically from the synthetic folic acid that is used in supplements and in food enrichment. The dietary reference intakes in the present advisory report are expressed as the amount of food folate. It has been assumed here that the figures for the bioavailability of food folate and the bioavailability of folic acid that is added to enriched foods are 50% and 15% lower, respectively, than the figure for the bioavailability of folic acid in supplements. One member of the Committee does not agree with this approach. He believes that the scientific knowledge for this distinction is insufficient and that the variation in bioavailability between the different types of folate in foods is too great. Therefore, he takes the view that the dietary reference intakes for folate should be expressed as the amount of synthetic folic acid.

The Committee's assessment of the folate status is based on the concentration of the vitamin in serum and red blood cells, as well as on the concentration of homocysteine in plasma. The Committee uses the last of the aforementioned factors as a status parameter, with 15 μmol/l as the upper limit of normal physiological distribution. A great deal of research is being conducted into the question of whether further reduction of plasma homocysteine concentration through increased folate intake provides protection against cardiovascular diseases. According to the Committee, this has currently not been sufficiently demonstrated because the required research results from interventional research are not yet available. However, this research is underway and the results are expected to be published within 2 to 3 years. If these publications become available, then the dietary reference intakes for folate must be re-evaluated. The Committee believes folate's possible protective effect against cancer has not been convincingly demonstrated.

The estimated average folate requirement for adults was determined on the basis of the three status parameters referred to above. A relatively high coefficient of variation of 25% was used in calculating the recommended dietary allowance because genetic factors also contribute to the variation in the folate requirement.* For all remaining groups, no estimated average requirement (and, therefore, no recommended dietary allowance) could be determined. The Committee therefore established adequate intakes for these groups. The derivation methods for infants, children, adolescents and lactating women correspond with those for vitamin B_6. The extra folate requirement during pregnancy was estimated to be 100 micrograms per day. The Committee maintains the advice to women who wish to become pregnant that — besides their normal intake in food — during the period from four weeks before to eight weeks after conceptionthey should also take a supplement containing 400 micrograms of folic acid to prevent neural tube defects.

Table S2 Dietary reference intakes for folate in micrograms per day.

(age) group	estimated average requirement[a]	recommended dietary allowance[a]	adequate intake[a]	tolerable upper intake level[b]
0 to 5 months	-	-	50	85
6 to 11 months	-	-	60	130
1 to 3 years	-	-	85	200
4 to 8 years	-	-	150	350
9 to 13 years	-	-	225	600
14 to 18 years	-	-	300	900
19 to 50 years	200	300	-	1,000
≥ 51 years	200	300	-	1,000
pregnant women	-	-	400[c]	1,000
lactating women	-	-	400	1,000

[a] the estimated average requirements, recommended dietary allowances and adequate intakes concern folate that occurs naturally in food

[b] the tolerable upper intake levels only relate to synthetic folic acid

[c] it is advisable that – besides their normal intake in food – during the period four weeks before to eight weeks after conception women should also take a supplement containing 400 micrograms of folic acid to prevent neural tube defects.

* The Committee refers here to people with the TT-genotype for 5,10-methylene tetrahydrofolate reductase, who require a higher level of folate. It is estimated that approximately 12% of Caucasians and Asians have this genotype; it apparently occurs less frequently in Afro-Americans.

The recommended dietary allowances for adults are lower than the values determined for the United States and for Germany, Switzerland and Austria, higher than the values for Great Britain and the European Union, and correspond with those for Scandinavian countries.

The Committee subscribes to the tolerable upper intake level for adults that the Health Council determined in 2000. This value corresponds with the values for the European Union and the United States. The upper limit was adjusted for the younger age groups on the basis of body weight.

Vitamin B_{12}

Vitamin B_{12} is involved in two enzyme systems in metabolism. Vitamin B_{12} has a direct influence on the metabolism of folate via one of the two systems. Vitamin B_{12} deficiency first manifests in tissues with a high division rate (such as red blood cells, blood platelets and epithelial cells of the gastrointestinal tract) but may also cause neurological damage.

The Committee believes there is insufficient scientific knowledge on the effect of intake on the status of vitamin B_{12} to serve as a basis for setting the standard. The Committee therefore takes the estimated average requirement for adults to be the amount of vitamin B_{12} that is required to compensate for daily losses of 0.2% of the minimum required bodily reserve of 500 micrograms, and assumes that the body takes up an average of 50% of the vitamin B_{12} in food. A coefficient of variation of 20% was assumed for the calculation of the recommended dietary allowance. The estimated average requirements and recommended dietary allowances for pregnant and lactating women, and the adequate intakes for all other groups, were derived with methods comparable to those described for vitamin B_6.

The recommended dietary allowance for adults is higher than the value in the United States because a higher coefficient of variation of the requirement was used in the present advisory report. The values in Scandinavia, Great Britain and the European Union are a little lower, and those in Germany, Switzerland and Austria are somewhat higher than the new Dutch values. These differences are attributable to differing assumptions about daily losses or the required size of the bodily reserves.

The Committee shares the opinions of expert committees in the United States and the European Union that no risks appear to be associated with taking higher doses of vitamin B_{12} and that the available data are not sufficient to enable a tolerable upper intake level to be derived for this vitamin.

Table S3 Dietary reference intakes for vitamin B_{12} in micrograms per day.

(age) group	estimated average requirement	recommended dietary allowance	adequate intake	tolerable upper intake level
0 to 5 months	-	-	0.4	-
6 to 11 months	-	-	0.5	-
1 to 3 years	-	-	0.7	-
4 to 8 years	-	-	1.3	-
9 to 13 years	-	-	2.0	-
14 to 18 years	-	-	2.8	-
19 to 50 years	2.0	2.8	-	-
$\geq$ 51 years	2.0	2.8	-	-
pregnant women	2.3	3.2	-	-
lactating women	2.7	3.8	-	-