Nutrition Research and Practice (2007), 2, 120-125


# Marginal folate inadequacy observed in a group of young children in Kwangju, Korea

Young-Nam Kim, Ji-Young Lee and Judy A. Driskell[§]
*Department of Nutrition and Health Sciences, University of Nebraska, Lincoln, NE 68583-0806, USA*

*Received March 5; Revised April 24, 2007; Accepted May 30, 2007*

## Abstract

Folate is important for multiple metabolic processes such as nucleic acid synthesis and interconversions, and cell division. Folate deficiency may be a risk factor for several pathologies, such as neural tube birth defects, dementia, and cardiovascular diseases. The objectives of this study were to estimate folate intakes and plasma concentrations of young children living in Kwangju, Korea. Three consecutive 24-h food recalls and fasting blood samples were obtained from 24 boys and 30 girls, aged 2-6 y, living in Kwangju, Korea. The daily folate intake (mean ± SD) of the children was $146.7 \pm 73.6\,\mu g$ dietary folate equivalents. No differences in folate intakes were observed by gender ($p \geq 0.05$). The mean folate intakes of the 2 and 3 y old groups were significantly lower ($p<0.05$) than those of 5 and 6 y old groups. Over half of subjects consumed <Korean Estimated Average Requirements for folate. The plasma folate concentration (mean ± SD) of all subjects was $19.2 \pm 8.7$ nmol/L, and there was no significant difference by age nor gender ($p \geq 0.05$). No significant correlation was observed between folate intakes and plasma folate concentrations. One subject (1.9%) in this study had a plasma folate concentration <6.8 nmol/L, which is indicative of folate deficiency. Approximately 24% of subjects had plasma folate concentrations of 6.8-13.4 nmol/L, which is representative of marginal folate status. In conclusion, some young children may have less than adequate folate status in Korea.

**Key Words: Folate, plasma folate, children, Korea, fortification**

## Introduction

Folate functions as a coenzyme in single-carbon transfers in the synthesis of the building blocks of DNA, thymidylate and purines, certain neurotransmitters, phospholipids, and hormones (Bailey & Gregory, 2006). Folate deficiency can cause abnormalities in single-carbon metabolism. These abnormalities (e.g. hyperhomocysteinemia or DNA hypomethylation) may result in deleterious consequences, including increased risk for certain types of chronic diseases and developmental disorders (Bailey & Gregory, 1999). Folate deficiency in childhood may affect the neural development of children. An inadequate folate intake leads to a decrease in serum and erythrocyte folate concentrations and an increase in plasma concentrations of homocysteine, and ultimately to macrocytic anemia (Institute of Medicine, 2000).

Several Korean studies have indicated that dietary intakes of folate of reproductive-aged women were insufficient and that a large portion of the women were marginally folate deficient (Hyun *et al.*, 1999; Lim *et al.*, 2000). Most of folate status studies conducted in Korea focused on childbearing women. Although a few studies (Lim, 1999; Shin *et al.*, 2005) have been conducted on the folate intakes of young Korean children, no study to date has reported biochemical measurements of plasma folate concentrations. Research is needed on the folate status of Korean young children. Therefore, the objectives of the present research were to estimate folate intakes and plasma concentrations of 2-6 y old children living in Kwangju, Korea.

## Subjects and Methods

### *Subjects*

Fifty-four seemingly healthy children aged 2-6 y in Kwangju participated in this study during the summer of 2005. Children who were not in good health, had any diseases interfering with folate metabolism, or took medications were not included in the study. The University of Nebraska-Lincoln Institutional Review Board approved the study, and informed consent was obtained from a parent of all participating children. All interviews were conducted by a trained interviewer in the Korean language.

### *Anthropometric measurements and dietary intake assessments*

Interviewers measured weights and heights of the subjects in light clothing without shoes. A trained Korean interviewer

[§] **Corresponding Author:** Judy A. Driskell, Tel. 1-402-472-8975, Fax. 1-402-472-1587, Email. jdriskell@unl.edu

**Table 1.** Selected characteristics of 2-6 y old Korean children living in Kwangju[1)]

| | 2 y (n=9) | 3 y (n=11) | 4 y (n=9) | 5 y (n=15) | 6 y (n=10) | Total (n=54) | Range of values |
|---|---|---|---|---|---|---|---|
| Anthropometry | | | | | | | |
| Height (cm) | 88.2 ± 6.2[a] | 101.2 ± 4.3[b] | 106.2 ± 3.8[c] | 113.3 ± 4.1[d] | 117.7 ± 5.2[e] | 106.3 ± 11.0 | (76.0 - 126.0) |
| Weight (kg) | 12.2 ± 2.0[a] | 16.6 ± 2.3[b] | 17.5 ± 2.5[bc] | 19.1 ± 1.6[c] | 21.1 ± 3.1[d] | 17.5 ± 3.6 | (9.9 - 27.8) |
| Intakes | | | | | | | |
| Energy (kcal/d) | 957 ± 200[a] | 1040 ± 238[a] | 1350 ± 360[b] | 1439 ± 199[b] | 1577 ± 297[b] | 1285 ± 339 | (625 - 2263) |
| Folate (μg DFE[2)]/d)[3)] | 97.4 ± 32.8[a] | 105.7 ± 56.7[a] | 135.4 ± 60.1[ab] | 190.2 ± 81.5[b] | 181.0 ± 68.7[b] | 146.7 ± 73.6 | (21.0 - 379.4) |
| Biochemical measurements | | | | | | | |
| Hemoglobin (g/L) | 123.7 ± 8.6[ab] | 120.0 ± 14.7[a] | 132.3 ± 5.8[ab] | 123.8 ± 7.8[a] | 126.2 ± 7.6[ab] | 124.9 ± 9.9 | (8.4 - 14.1) |
| Hematocrit (%) | 37.2 ± 2.6[ab] | 36.0 ± 3.8[a] | 39.5 ± 1.8[b] | 36.8 ± 1.9[a] | 37.7 ± 2.1[ab] | 37.3 ± 2.7 | (27.7 - 42.4) |
| Plasma folate (nmol/L) | 22.7 ± 12.5 | 16.5 ± 7.9 | 19.3 ± 8.4 | 20.4 ± 8.6 | 16.8 ± 5.6 | 19.2 ± 8.7 | (6.0 - 48.3) |

1) Values are means ± SD except the last column which is the range of values of all subjects.
abcde Values with the same superscript in the row were not significantly different, p > 0.05, by Least Significant Difference multiple range test.
2) DFE: dietary folate equivalents.
3) One 4 y old boy and a 5 y old boy in this study took supplements containing 0.2 μg folic acid daily.

obtained 3 consecutive 24-h food recalls (2 weekdays and 1 weekend day) from a parent of each subject using food models and cross-checking (Gibson, 2005). A computer-aided nutritional analysis program developed by the Korean Nutrition Society (The Korean Nutrition Society, 2002) was used in estimating energy, protein, carbohydrate, total fat, and folate intakes. Also, the program was used in determining the major food sources of folate of the subjects by food groups.

### *Collection of blood samples and laboratory analyses*

Venous blood samples (~ 5 mL) were collected from children following an overnight fast in EDTA-containing vacutainers. The EDTA-containing tubes were kept in crushed ice and were protected from light throughout handling and processing. Blood samples were centrifuged at 3000 ×g at 5℃ for 10 min. Plasma was transferred into airtight tubes, frozen at −70℃, and transported to the University of Nebraska-Lincoln, NE, USA in dry ice. After arriving in the USA laboratory, plasma samples were stored at −70℃ for future analyses of plasma folate concentrations.

Hemoglobin and hematocrit were measured using an automated cell counter, ADVIA 120 (Bayer Diagnostics, Tarrytown, NY, USA) at Green Cross Reference Laboratory in Yougin, Korea. Plasma concentrations of folate were analyzed using the SimulTRAC-SNB Radioassay Kit (ICN Diagnostics, Orangeburg, NY, USA). Anemia was defined a priori as hemoglobin <110 g/L and <115 g/L for those children aged 2-4 y old and 5-6 y old, respectively, and also defined as hematocrit <33% for 2-4 y olds and <34% for 5-6 y olds (Stoltzfus & Dreyfuss, 1998). The reference ranges for plasma folate were <6.8 nmol/L for deficient, 6.8-13.4 nmol/L for marginal, and >13.4 nmol/L for adequate status (Sauberlich, 1975).

### *Statistical analysis*

The data were analyzed by gender and age using SAS version 9.1.3 (SAS Institute, Inc., Cary, NC). The differences between genders and among age groups were analyzed using 1-way ANOVA with the Least Significant Difference post-hoc test (Rosner, 2000). Pearson correlation coefficients were utilized to determine correlations between intakes and plasma concentrations of folate and between these two parameters and both hemoglobin and hematocrit values. Differences were considered significant at $p<0.05$. Values in the text are means ± SD.

## Results

Boys (n=24) and girls (n=30), 2-6 y old, living in Kwangju participated in this study, with the mean age being 4.1 y. The characteristics of the subjects are presented in Table 1. No differences in any of these characteristics of the subjects were observed by gender ($p \geq 0.05$). The mean (± SD) heights of 2 y, 3-5 y, and 6 y old children as categorized using the age groupings of the Korean Dietary Reference Intakes (DRIs) (The Korean Nutrition Society, 2005) were 88.2 ± 6.2, 107.7 ± 6.6, and 117.7 ± 5.2 cm, respectively, and their mean (± SD) weights were 12.2 ± 2.0, 17.9 ± 2.3, and 21.1 ± 3.1 kg, respectively. The mean energy intakes of 2 and 3 y old children were significantly lower ($p<0.05$) than those of 4, 5, and 6 y old children (Table 1). The mean (± SD) energy intakes of 2 y, 3-5 y, and 6 y old children were 957 ± 200, 1286 ± 305, and 1577 ± 297 kcal/d, respectively. The mean (± SD) intakes of proteins, carbohydrates, and total fats of the subjects were 48.6 ± 16.8, 192.9 ± 51.3, and 38.1 ± 14.5 g/d, respectively. Approximately 74% of the subjects met the Korean Acceptable Macronutrient Distribution Range (The Korean Nutrition Society, 2005) for carbohydrates, 93% for proteins, and 69% for total fats. The majority of the subjects reported that their intakes were typical. In this study, 9.3% of children had hemoglobin values of <cutoffs used to define anemia. The mean (± SD) values of hemoglobin of 2 y, 3-5 y, and 6 y olds were 123.7 ± 8.6, 124.7 ± 14.5, and 126.2 ± 7.6 g/L, respectively. In that they had hematocrit values <cutoffs, 7.4% of subjects were anemic. The mean (± SD) hematocrit values by Korean DRIs age groupings were as follows: 37.2 ± 2.6, 2 y olds;

37.3 ± 2.9, 3-5 y olds; and 37.7 ± 2.1%, 6 y olds.

Mean dietary intakes and plasma concentrations of folate in the children are also given in Table 1. No significant differences in folate intakes and plasma concentrations were observed by gender ($p \geq 0.05$). The mean (± SD) folate intake of the subjects was 146.7 ± 73.6 $\mu$g dietary folate equivalents (DFE)/d. One 4 y old boy and a 5 y old boy in the current study consumed supplements containing 0.2 $\mu$g folic acid daily. Mean (± SD) folate intakes of 2 y, 3-5 y, and 6 y old children were 97.4 ± 32.8, 149.5 ± 77.0, and 181.0 ± 68.7 $\mu$g DFE/d, respectively. The folate intakes of these 2 boys were >Korean Estimated Average Requirement (EAR) and plasma concentrations of the boys were >13.4 nmol/L, which is indicative of adequate folate status. The mean folate intakes of 2 and 3 y old children were significantly lower ($p<0.05$) than those of 5 and 6 y old children. The mean plasma folate concentration of all subjects combined was 19.2 ± 8.7 nmol/L, and there was no significant difference by age ($p \geq 0.05$). Mean (± SD) plasma concentrations of folate of 2 y, 3-5 y, and 6 y old children were 22.7 ± 12.5, 18.9 ± 8.3, and 16.8 ± 5.6 nmol/L, respectively. There was no significant correlation between folate intakes and plasma folate concentrations ($p \geq 0.05$). Also, no significant correlation was observed between plasma folate concentrations and hemoglobin and hematocrit values of the subjects in this study. Currently a few milk manufacturers in Korea add folate to some of the milk products they produce. The parents of all but 9 subjects reported the brand and type of milk consumed by their children, and these products did not contain added folate. Of these 9 subjects, one subject had a plasma folate concentration indicative of deficiency and two subjects (5 y old girl and 6 y old boy) had concentrations indicative of marginal folate status.

Fruits and vegetables provided 42% of the daily folate intake followed by grain products including flours at 36%. Meats, fish, eggs, and beans provided 14%; milk and milk products, 5%; and fats, seeds, and sweets, 3%. The predominant folate food sources, consumed by the children in the summer of 2005, were kimchi, toasted laver, cooked rice, eggs, watermelons, tomatoes, and muskmelons. Subjects reportedly consuming <Korean DRIs for folate got 42% of their folate from grain products including flours, 34% from fruits and vegetables, 14% from meats, fish, eggs, and beans, 7% from milk and milk products, and 3% from fats, seeds, and sweets. Subjects reportedly consuming ≥Korean folate DRIs got 31% of their folate from grain products including flours, 48% from fruits and vegetables, 14% from meats fish, eggs, and beans, 4% from milk and milk products, and 3% from fats, seeds, and sweets.

The percentages of subjects with less than adequate folate status using various criteria are given in Fig. 1. Fifty-seven percent of subjects consumed EARs for folate; this was 78% of 2 y, 51% of 3-5 y, and 66% of 6 y old subjects. Almost 60% of the children in this study consumed <folate EARs for USA/Canadians. One boy in the 4 y old group was folate deficient based on his having a plasma folate concentration <6.8 nmol/L (Sauberlich, 1975). Plasma folate concentrations of 24.1% of the subjects were between 6.8 and 13.4 nmol/L, which is representative of marginal folate status (Sauberlich, 1975). The percentages of subjects having marginal folate status subjects by Korean DRIs age groupings were as follows: 11%, 2 y; 26%, 3-5 y; and 33%, 6 y olds.

## Discussion

Dietary intakes and plasma concentrations of folate were determined in 54 healthy children living in Kwangju, Korea. The mean weight and height values of the children in the present study were similar to the means of USA children (Ogden *et al.*, 2004) and Japanese children (Natsuchita *et al.*, 2004). In the current study, 9.3% and 7.4% of the subjects had hemoglobin values and hematocrit values, respectively, <cutoffs used to define anemia, which were in line with the prevalence of anemia among preschool children in Korea (5.4%) (Park *et al.*, 2005) and USA 2-5 y old children (12%) (Polhamus *et al.*, 2004). Anemia is an indicator of poor nutrition and poor health (World Health Organization/United Nations Children's Fund, 2004). Thus, most of the Korean children in the present study were in apparent good health.

In the present study, the mean folate intake (146.7 $\mu$g DFE/d) was similar to the mean intakes of Spanish children aged 2-5 y old in the enKid Study, 1998-2000 (131.5 $\mu$g/d) (Serra-Majem *et al.*, 2006), and German children aged 2-3 y and 4-6 y old in the Dortmund Nutritional and Anthropometric Longitudinally Designed Study (135.5 $\mu$g/d and 180.5 $\mu$g/d, respectively) (Sichert-Hellert & Kersting, 2004). However, the mean folate intake in the current study was lower than median folate intakes of USA children aged 1-5 y in the Third National Health and Nutrition Examination Survey (NHANES III), 1988-1994 (400 $\mu$g/d) (Lewis *et al.*, 1999); this survey was conducted prior to mandatory fortification of enriched grain products by the Food and Drug Administration (FDA) in the USA. Fifty-seven percent of the subjects as categorized using the Korean DRIs age groupings consumed <EARs for folate for Koreans (The Korean Nutrition Society, 2005), and 59% of subjects consumed <USA/Canadian EARs (Institute of Medicine, 2000). The majority of USA children included in NHANES III consumed >USA/Canadian EARs for folate (Lewis *et al.*, 1999). In Germany, 4.2% of 1-3 y old children (n=124) and 18% of 4-6 y old children (n=47) consumed <folate EARs for USA/ Canadians (Kersting *et al.*, 2000). Thus, the prevalence of inadequate folate intakes (<EARs) of Korean children in the present study was higher than those of other countries prior to fortification of grain products.

The accuracy of food composition data is important in estimating the intakes and adequacies of nutrients for population groups (Scrimshaw, 1997). Due to the limitations of traditional analytical methods, including the use of folate conjugase as the

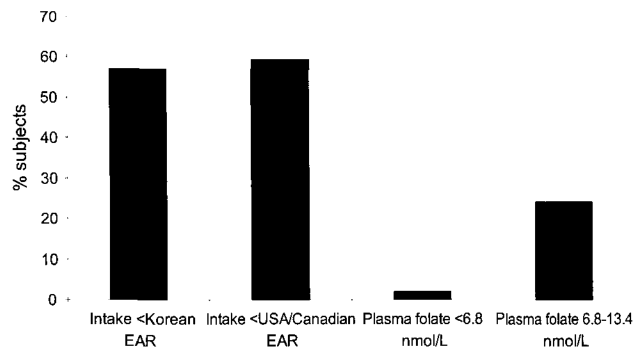


**Fig. 1.** Percentages of 2-6 y old children having values indicative of inadequate folate status using various criteria
EAR: Estimated Average Requirement. References for the criteria are as follows: <Korean EAR (The Korean Nutrition Society, 2005), <USA/Canadian EAR (Institute of Medicine, 2000), <6.8 nmol/L for deficient, 6.8-13.4 nmol/L for marginal, and >13.4 nmol/L for adequate status (Sauberlich, 1975).

only enzyme, used in generating the food composition data for folate, the current database values underestimate actual folate contents. Several years ago, researchers started using trienzyme extraction (amylase and protease treatments in addition to folate conjugase) as the recommended method for measuring food folate content (Puwastien *et al.*, 2005). It has been reported that current food folate composition data in Korea provides underestimations of folate intake of the Korean population (Han *et al.*, 2005; Hyun & Han, 2001). According to the research of Han *et al.* (2005), folate intakes of college students (n=106) calculated using analyzed folate values were 1.8 times higher than the intakes calculated using the current Korean food composition database. Also, an average folate loss of 29% was indicated by cooking (Han *et al.*, 2005). For the reasons indicated above, it is likely that estimates of folate intakes in this study could be underestimates of actual intakes.

In the current study, major contributors of folate intake were fruits and vegetables providing 42% of the daily folate intake and grain products including flours supplied 36%. In a study of folate intake conducted by Han *et al.* (2005), vegetables were the major folate source contributing 38-44% of intake of Korean college students. Among vegetables, kimchi was predominant folate source in the study of Han *et al.* (2005). In the current study, the predominant folate food sources, consumed by the children during summer, 2005, were kimchi, toasted laver, cooked rice, eggs, watermelons, tomatoes, and muskmelons, which are similar with the major folate food sources of Korean college students (Han *et al.*, 2005). Rice is a staple food in Korea. Although the folate content of rice (12 $\mu$g/100g; The Korean Nutrition Society, 2002) is not as a high as those of vegetables, a group of grain products and flours including rice provided a considerable portion of the folate intake of the Korean children of the current study.

The mean plasma folate concentration of Korean children aged 2-6 y was 19.2 nmol/L, which is higher than the mean of 2-5 y old Austrian children (10 nmol/L) (Huemer *et al.*, 2006), but in line with the mean of 2-5 y old Dutch children (24 nmol/L) (van Beynum *et al.*, 2005) and the median (21 nmol/L) of 4-8 y old USA children in NHANES III, 1988-1994 (Institute of Medicine, 2000). One subject (1.9%) in this study had a plasma folate concentration <6.8 nmol/L, which is indicative of folate deficiency (Sauberlich, 1975). In the Mexican National Survey of 1999, approximately 5% of the children were folate deficient (Villalpando *et al.*, 2003), and 2% of Costa Rican children <6 y old were folate deficient (Allen, 2004). Sixteen percent of USA children aged ≤5 y old in NHANES III had serum folate concentrations indicative of deficiency (Pfeiffer *et al.*, 2005). Approximately 24% of subjects in the current study had plasma concentrations of 6.8-13.4 nmol/L, which is interpreted as marginal status of folate (Sauberlich, 1975). The prevalence of marginal folate status of children in this study was higher than that of Guatemalan children (1%) aged 8-12 y (Rogers *et al.*, 2003), and that of Costa Rican children (9%) <6 y old (Allen, 2004).

Folate fortification may be of benefit to women of childbearing age in increasing their intake of folate and thereby reduce their risk of a pregnancy affected by a neural tube birth defect. Also, the fortification may improve folate nutrition for the general population (Institute of Medicine, 2000). In the USA, FDA has required since 1998 that enriched grain products be fortified with folic acid at a concentration of 140 $\mu$g/100 g cereal grain (Food and Drug Administration, 1996), and the folate status of the USA population has improved as indicated by increased plasma folate and red blood cell concentrations (Ganji & Kafai, 2006; Pfeiffer *et al.*, 2005). The median folate intake of 1-5 y old USA children in NHANES III 1988-1994, prior to folate fortification was 400 $\mu$g DEF/d (Lewis *et al.*, 1999), while in NHANES 2001-2002, after folate fortification, the median intakes of 1-3 and 4-8 y old USA children were 369 $\mu$g DFE/d and 501 $\mu$g DFE/d, respectively (Moshfegh *et al.*, 2005). The prevalence of deficient serum folate concentrations (<6.8 nmol/L) decreased from 16% in NHANES III 1988-1994 to 0.5% in NHANES 1999-2000 for the USA population (Pfeiffer *et al.*, 2005). Also, the prevalence of neural tube birth defects decreased by 19% in USA, when pre-folic acid fortification data were compared with the post-folic acid fortification data (Honein *et al.*, 2001). Australia, Chile, Hungary, and New Zealand are fortifying >200 $\mu$g folate in 100 g flour (Oakely *et al.*, 2004). However, in Korea, folate fortification is not currently required in food products. Whole grains are imported for use in manufacturing 98% of the flours consumed in Korea (Woo, 2006), and the manufacturers typically do not add folate during processing. Some food companies in Korea have fortified folate voluntarily along with other nutrients in their breakfast cereal products, milk, and soymilk. The parents of most milk and soymilk drinkers in this study indicated that their children drank non-fortified milk or soymilk. In this study, none of the subjects consumed any breakfast cereal products. Subjects consuming <Korean EARs for folate got more of their folate from grain products including flours than subjects reporting

consuming ≥Korean EARs for folate. According to Han *et al.* (2005), 19-36% folate losses were indicated during the cooking of grain products which are one of major folate sources. Therefore, folate fortification of grain products including flours may improve folate intakes and plasma concentrations of Korean children, women of childbearing age, and the population in general.

In conclusion, approximately 60% of subjects had inadequate folate intakes, that is <Korean folate EARs. Although the prevalence of folate deficiency was low based on plasma concentrations <6.8 nmol/L, one-quarter of Korean children in the current study had marginal status of folate, which is higher than the prevalence of many other countries. Some young children in Korea may be at risk of inadequate folate status. Thus, increased consumption of folate-rich foods such as liver, yeast, legumes, dark green leafy vegetables, and fortified food products such as breakfast cereals, milk, and soymilk can improve the folate status of young children in Korea. The grain product intakes of young children in the current study were considerable. Folate fortification of grain products would most likely improve the folate status of Korean children, as well as other population groups.

## Acknowledgment

A contribution of the University of Nebraska Agricultural Research Division, supported in part by funds provided through the Hatch Act. The authors are thankful to Dr. Youn-Ok Cho, Professor of Food and Nutrition, Duksung Women's University, Seoul, Korea, for her suggestions in performing this study in Korea. The authors also thank Young-Ki Park, Research Technologist of Nutrition and Health Sciences, University of Nebraska-Lincoln, USA, for technical assistance.

## Literature cited

Allen LH (2004). Folate and vitamin $B_{12}$ status in the Americas. *Nutr Rev* 62:29-33.

Bailey LB & Gregory JF 3rd (2006). Folate. In: Bowman BA & Russell RM (Eds.), *Present Knowledge in Nutrition, 9th ed.*, p. 278-301. ILSI press, Washington, DC. USA

Bailey LB & Gregory JF 3rd (1999). Folate metabolism and requirements. *J Nutr* 129:779-782.

Food and Drug Administration (1996). Food standards: amendment of standards of identity for enriched grain products to require addition of folic acid. *Fed Regist* 61:8781-8797.

Ganji V & Kafai MR (2006). Trends in serum folate, RBC folate, and circulating total homocysteine concentrations in the United States: analysis of data from National Health and Nutrition Examination Survey, 1988-1994, 1999-2000, and 2001-2002. *J Nutr* 136:153-158.

Gibson RS (2005). *Principles of Nutritional Assessment, 2nd ed.* Oxford Press, New York. USA

Han YH, Yon M & Hyun TH (2005). Folate intake estimated with an updated database and its association to blood folate and homocysteine in Korean college students. *Eur J Clin Nutr* 59: 246-254.

Honein MA, Paulozzi LJ, Mathews TJ, Erickson JD & Wong LYC (2001). Impact of folic acid fortification of the US food supply on the occurrence of neural tube defects. *JAMA* 285:2981-2986.

Huemer M, Vonblon K, Födinger M, Krumpholz R, Hubmann M, Ulmer H & Simma R (2006). Total homocysteine, folate, and cobalamin, and their relation to genetic polymorphisms, lifestyle and body mass index in healthy children and adolescents. *Pediatr Res* 60:764-769.

Hyun TH & Han YH (2001). Comparison of folate intake and food sources in college students using the 6th vs 7th nutrient database. *Korean Journal of Nutrition* 34:797-808.

Hyun T, Han YH & Lim EY (1999). Blood folate level determined by a microplate reader and folate intake measured by a weighted food record. *Korean Journal of Community Nutrition* 4:512-520.

Institute of Medicine (2000). *Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin $B_6$, Folate, Vitamin $B_{12}$, Pantothenic Acid, Biotin, and Choline.* National Academy Press, Washington, DC, USA

Kersting M, Alexy U & Sichert-Hellert W (2000). Vitamin intake of 1- to 18-year-old German children and adolescents in the light of various recommendations. *Int J Vit Nutr Res* 70:48-53.

Lewis CJ, Crane NT, Wilson DB & Yetley EA (1999). Estimated folate intakes: data updated to reflect food fortification, increased bioavailability, and dietary supplement use. *Am J Clin Nutr* 70: 198-207.

Lim HJ (1999). A study on the food habit and the evaluation of nutrient intake of preschool children in Pusan. *J Korean Soc Food Sci Nutr* 28:1369-1379.

Lim HS, Jin HO & Lee JA (2000). Dietary intakes and status of folate in Korean women of child-bearing potential. *Korean Journal of Nutrition* 33:296-303.

Matsushita Y, Yoshiike N, Kaneda F, Yoshita K & Takimoto H (2004). Trends in childhood obesity in Japan over the last 25 years from the National Nutrition Survey. *Obes Res* 12:205-214.

Moshfegh A, Goldman J & Cleveland L (2005). What we eat in America, NHANES 2001-2002: usual nutrient intake from food compared to Dietary Reference Intakes. U.S. Department of Agriculture, Agricultural Research Service. http://www.ars.usda.gov/SP2UserFiles/Place/12355000/pdf/usualintaketables2001-02.pdf. Accessed on 1/14/2007.

Oakely GP Jr, Bell KN & Weber MB (2004). Recommendations for accelerating global action to prevent folic acid-preventable birth defects and other folate-deficiency diseases: meeting of experts on preventing folic acid-preventable neural tube defects. *Birth Defects Res A Clin Mol Teratol* 70:835-837.

Ogden CL, Fryar CD, Carroll MD & Flegal KM (2004). Mean body weight, height, and body mass index, United States 1960-2002. *Advance Data* 27:1-17.

Park HS, Shin KO & Yoo YY (2005). Study on the effect of food habits and nutritional status on anemia in Korean preschool children. *FASEB J* 19:434[Abstract].

Pfeiffer CM, Caudill SP, Gunter EW, Osterloh J & Sampson EJ (2005). Biochemical indicators of B vitamin status in the US population after folic acid fortification: results from the National Health and Nutrition Examination Survey 1999-2000. *Am J Clin Nutr* 82:442-450.

Polhamus B, Dalenius K, Thompson D, Scanlon K, Borland E, Smith B & Grummer-Strawn L (2004). Pediatric nutrition surveillance 2003 report. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention. http://www.cdc.gov/pednss/pdfs/PedNSS_2003_Summary.pdf. Accessed on 3/5/2007.

Puwastien P, Pinprapai N, Judprasong K & Tamura T (2005). International inter-laboratory analyses of food folate. *J Food Comp Anal* 18:387-397.

Rogers LM, Boy E, Miller JW, Green T, Sabel JC & Allen LH (2003). High prevalence of cobalamin deficiency in Guatemalan schoolchildren: associations with low plasma holotranscobalamin II and elevated serum methylmalonic acid and plasma homocystein concentrations. *Am J Clin Nutr* 77:433-440.

Rosner B (2000). *Fundamentals of Biostatistics, 5th ed.* Duxbury, Pacific Grove, CA. USA

Sauberlich HE (1975). Detection of folic acid deficiency in populations. In: Food and Nutrition Board (Eds.), *Folic acid: Biochemistry and Physiology in Relation to the Human Nutrition Requirement*, p.213-231. National Academy of Sciences, Washington, DC. USA

Scrimshaw NS (1997). INFOODS: the international network of food data systems. *Am J Clin Nutr* 65:1190-1193.

Serra-Majem L, Ribas-Barba L, Pérez-Rodrigo C & Bartrina JA (2006). Nutrient adequacy in Spanish children and adolescents. *Br J Nutr* 96:49-57.

Shin KO, Yoo YY & Park HS (2005). Study on the eating habits and growth development in Korean preschool children. *Korean Journal of Nutrition* 38:455-464.

Sichert-Hellert W & Kersting M (2004). Fortifying food with folic acid improves folate intake in German infants, children, and adolescents. *J Nutr* 134:2685-2690.

Stoltzfus RJ & Dreyfuss ML (1998). *Guidelines for the Use of Iron Supplements to Prevent and Treat Iron Deficiency Anemia.* INACG/WHO/UNICEF, Washington, DC. USA

The Korean Nutrition Society (2002). *Computer Aided Nutritional Analysis Program for Professionals.* The Korean Nutrition Society, Seoul. Republic of Korea

The Korean Nutrition Society (2005). *Dietary Reference Intakes for Koreans*. Kookjin, Seoul. Republic of Korea

van Beynum ID, den Heijer M, Thomas CMG, Afman L, Oppenraay-van Emmerzaal D & Blom H (2005). Total homocysteine and its predictors in Dutch children. *Am J Clin Nutr* 81:1110-1116.

Villalpando S, Montalvo-Velarde I, Zambrano N, Garcia-Guerra A, Ramirez-Silva CI, Shamah-Levy T & Rivera JA (2003). Vitamin A, C, and folate status in Mexican children under 12 years and women 12-49 years: a probabilistic national survey. *Salud Pub Mex* 45:508-519.

World Health Organization/United Nations Children's Fund (2004). Focusing on anaemia, towards an integrated approach for effective anaemia control. World Health Organization. http://www.who.int/topics/anaemia/en/who_unicef-anaemiastatement.pdf. Accessed on 3/5/2007.

Woo SH (2006). *Our Flour to Our Children.* The Seoul Newspaper, Seoul. Republic of Korea