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EFFECTS OF VITAMIN A DEFICIENCY ON HEPATIC FOLATE METABOLISM IN RATS. B. Fell and R.D. Steele. University of Wisconsin, Madison, WI 53706.

Hepatic folate metabolism was studied in vitamin A-deficient rats (-A) and pair-fed controls (+A). Liver retinol of all -A was less than 1.5 μg/g. -A oxidized 16% less (P<.01) of a 400 mg [ring-2-^{14}C]histidine (HIS) load to $^{14}CO_2$ and excreted 4.7 times as much (P<.05) urinary formiminoglutamate (FIGLU) as +A in 24 hr. While the activity of hepatic FIGLU transferase, which catabolizes FIGLU using tetrahydrofolate (THF) as cofactor, was unaffected by the vitamin A deficiency, hepatic THF levels in -A given a HIS load were decreased by 58% (P<.01), demonstrating that less THF was available for FIGLU metabolism in -A. Concomitantly, 5-methyl-THF (meTHF) levels increased by 39% (P<.01) in -A while formyl-THF and total folate levels were similar to +A. -A exhibited a 43% loss (P<.01) in activity of hepatic 10-formyl-THF dehydrogenase, which generates both THF and the $^{14}CO_2$ from labeled HIS, while 5,10-methylene-THF reductase activity, which generates meTHF, was increased by 81% (P<.01) in -A. The results suggest that vitamin A deficiency produces selective changes in the activities of hepatic folate-dependent enzymes which, after a HIS load, bring about an altered distribution of folate cofactors and a decreased THF concentration relative to +A. This would account for the impaired HIS oxidation and elevated FIGLU excretion in -A. (Supported by USDA Grant #82-CRCR-1-1153, College of Ag. & Life Sciences and The Graduate School.)

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ASSOCIATION BETWEEN FOLACIN STATUS AND SCHOOL PERFORMANCE IN ADOLESCENTS. J. C. Tsui, J. W. Nordstrom and M. B. Kohrs. Human Nutrition Research Program, Lincoln University, Jefferson City, MO 65101.

The relationship of folacin status to school performance was investigated in 308 adolescents ages 11-16 years attending junior high schools in Kansas City, Missouri. Folacin status was assessed by measuring folate levels in blood and in diets. Grade Point Average (GPA) was used as an index of school performance. Positive correlations between GPA and serum folate (r=0.29, p< 0.001) and red cell folate (r=0.14, p< 0.05) were observed. Moreover, the subjects who had serum folates below 3.0 ng/ml had a significantly (p< 0.001) lower mean GPA than those who had serum folates above 3.0 ng/ml. Also, the mean GPA of subjects with red cell folates less than 200 ng/ml was significantly (p< 0.01) lower than those with red cell folates more than 200 ng/ml. The GPA scores were not related to dietary intakes of folate or of other nutrients, based on 7-day food records. Hematological indices and other biochemical parameters were also tested statistically in relation to GPA scores; however, no relationships were found. The results indicated that folacin levels in blood serum and red cells were the only nutritionally related factors positively associated with school performance in adolescents. (Supported by USDA Grant #OH82-504).

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ALTERED RELATIONSHIP BETWEEN RED CELL AND SERUM FOLATE IN THE AGED, SUGGESTING IMPAIRED ERYTHROCYTE FOLATE TRANSPORT. Susan Ettinger and Neville Colman. Bronx VA Med Ctr. Mount Sinai School of Med. Columbia U. NY; Hahnemann U. Phila. PA.

We reported (Clin Res 32:686A. 1984) inability to confirm prior reports that folate deficiency is more common in the aged. Using rigorous methods to exclude relevant underlying conditions, we actually found mean serum and red cell folates significantly higher in aged subjects. To explore possible mechanisms for this observation, we administered 2 mg oral folic acid daily for two weeks to two groups of screened subjects representing young (22-43 yrs) and elderly (67-90 yrs) age groups with similar initial levels of serum folate (8.5±2.4 vs. 8.0±3.7 ng/ml) and red cell folate (455±73 vs. 385±152 ng/ml). Serum folate rose only 2.0-fold in the young but 3.7-fold in the elderly. In contrast, erythrocyte folate rose by 45% in the young compared with only 28% in the aged. Consequently, differences were greatest when expressing serum folate as a percentage of red cell folate to compare the utilization of circulating folate.

	Baseline	7 days	14 days
Young (SF/RCF%)	1.8±0.3	4.9±1.1	4.0±0.8
Aged (SF/RCF%)	2.2±0.7	7.6±2.8	8.1±2.8

Although similar at day 0, the difference was significant at day 14 (p<0.01). This may reflect impaired transport of supplemental folate from serum into erythroid precursors of the aged, and may contribute to frequent folate deficiency observed in those with relevant underlying conditions.

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RENAL FOLATE ABSORPTION AND THE KIDNEY FOLATE BINDING PROTEIN (FBP). MICROPUNCTURE INFUSION STUDIES. J. Selhub, F. Carone and S. Nakamura. (SPON: I.H. Rosenberg) Univ. of Chicago and Northwestern Univ., Chicago, IL 60637 U.S.A.

The brush border membrane of proximal tubule contains a high concentration of FBP with affinity for folic acid > 5-CH_3-THF >> methotrexate. In the present studies we employed micropuncture infusion of surface proximal tubule of kidneys in rats to assess if FBP is involved in renal tubular folate absorption. The surface tubules were microinfused with pH 7.4 buffered solutions containing known amounts of [^{3}H]folic acid and [^{14}C]inulin. Urine collected was analysed for radioactivity contents to determine net [^{3}H]folic acid tubular uptake. The data obtained indicate that folate absorption is confined primarily to the proximal convoluted tubule of the nephron. Absorption is saturable and structure specific, with activity for folic acid > 5-CH_3THF >> methotrexate. Following microinfusion with a saturating dose of unlabelled folic acid, the half life for the regeneration of surface folate uptake sites is in the range of 7-12 min. Data obtained from the measurement of [^{3}H] that remains in the kidney tissue at various time periods after microinfusion, suggest that the half life for the transcellular flux is 44 min. These data suggest that renal tubular folate absorption begins with binding to luminal FBP and is followed by internalization and transport of the substrate into the blood. How the surface bound folate enters into the tubular cell and then exits into the blood remains to be determined.

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SOME EFFECTS OF VITAMIN AND MINERAL SUPPLEMENTATION IN HEALTHY YOUNG WOMEN. G. A. Spiller, T. S. Pattison, C. D. Jensen, L. G. Wong, J. H. Whittam and J. Scala. Shaklee Research Center, Hayward, CA 94545.

Forty two healthy young women attending Mills College (Oakland,Ca) and consuming their meals in the college cafeteria were randomized in two balanced double-blind groups and fed for 11 weeks either a placebo or a vitamin-mineral supplement (VMS) (Vita-Lea, Shaklee Corp., San Francisco, Ca) supplying approximately the USRDA (United States Recommended Dietary Allowance) of all vitamins, zinc, iron, iodine and copper and 60% USRDA of calcium, 50% USRDA of magnesium and 45% USRDA of phosphorus. Serum and hematological values were determined after 11 weeks and compared to pre-treatment values which had been determined after at least 30 days without any VMS. Mean serum levels of vitamins B12 and C and folate increased from baseline on VMS: B12 +25 pg/ml, C +0.53 mg/dl, folate +7.40 ng/ml , all with p < 0.05, while there was no change for the placebo group. There were no significant (p > 0.05) serum changes in either group for vitamins A and E or any of the VMS minerals. Serum ferritin and red cell folate showed an increase for subjects who were below normal levels before supplementation, but mean changes were not significant (p > 0.05). There were no significant changes in any standard hematological values and no biochemical aberrations in the routine serum chemistry determinations (p > 0.05). The health significance of the biochemical changes found needs further study.

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DIETARY VITAMIN B_6 AND HOMOCYSTEINE LEVELS IN MEN AT LOW AND HIGH RISK FOR CORONARY HEART DISEASE (CHD). M. Swift and T.D. Shultz. Departments of Biochemistry and Nutrition, School of Medicine, Loma Linda University, Loma Linda, CA 92350.

Pyridoxal phosphate acts as a cofactor in the conversion of homocysteine (H) to cystathionine. Animals deficient in dietary vitamin B_6 (DB6) accumulate H, in some species, possibly increasing the risk of CHD. To explore this relationship further, we assessed the interrelation of DB6 with plasma H levels. Fasting bloods were obtained from 9 men at low risk (LR) and 5 at high risk (HR) for CHD. Each HR subject met at least 2 major risk factors. HR mean systolic blood pressure, total cholesterol (TC), and TC/HDL-cholesterol ratios were significantly higher than LR levels (p<0.05, p<0.001, p<0.001, respectively). Groups were comparable by age, weight, height, skinfolds, exercise and smoking history. Plasma free and protein bound H were analyzed by HPLC separation and electrochemical detection. TC and HDL-cholesterol were determined enzymatically. DB6 intakes were estimated from a 3-day diet record, and were similar, providing 84% (LR) and 69% (HR) of the RDA. No significant difference was found for bound H between groups; however, mean free H (μmol/l) differed significantly between LR (3.49±1.30) and HR (5.57±0.74) subjects. There were significant negative correlations between DB6 and bound H levels for the HR and combined (LR, HR) groups (r=-0.71, p<0.005; r=-0.49, p<0.05, respectively). These data suggest that bound and perhaps free H levels may be decreased by increased DB6 intake in humans.

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