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EFFECTS OF BETA-CAROTENE AND HYPERVITAMINOSIS A ON DETOXIFICATION ENZYMES. G.V. Mitchell, S.R. Biskely, E. Grundel & N.Y. Jenkins. Food and Drug Administration, Washington, DC 20204.

The ability of beta-carotene to enhance or alleviate the effects of hypervitaminosis A on hepatic phase I and phase II detoxification enzyme systems was investigated. Male weanling Sprague-Dawley rats, 10/group, were fed ad libitum for 8 weeks varying levels of vitamin A and beta-carotene in a 3 x 3 factorial experimental design. Vitamin A was fed as retinyl palmitate at 2.2 (ctrl), 22 (RP1), and 220 (RP2) mg/kg of diet. Each of these groups was fed with beta-carotene at either 0, 48 (BC1), or 480 (BC2) mg/kg of diet. Phase I detoxification was determined by measuring cytochrome P-450 in reduced microsomes and by assaying the specific activity of microsomal benzphetamine demethylase. Phase II detoxification was determined by assaying glutathione-S-transferase (GST) activity of liver cytosol. Cytochrome P-450 levels and demethylase activity were significantly lower in the RP2-fed groups than in the other groups. GST activity, with 1-chloro-2,4-dinitrobenzene as the substrate, was significantly higher in the RP2-fed groups. These findings suggest that hypervitaminosis A causes changes in the phase I and phase II detoxification enzyme systems in the liver of rats. Although these detoxification systems did not appear to be affected by beta-carotene, the contribution of carotene to liver vitamin A might have been a factor in the changes observed in RP2-fed groups.

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EFFECT OF GRADED LEVELS OF BETA-CAROTENE ON SKIN YELLOWING IN HEALTHY HUMANS. G. Spiller, C. Jensen, A. Drunkert and J. Whittas. Shaklee Research Center, Hayward, CA 94545.

In view of the interest in the possible cancer-preventing properties of beta-carotene (BC), the dose at which skin yellowing begins to occur on BC needs to be quantified. In this 12-week dose response, double-blind, parallel study, 40 healthy adult males and females were assigned to one of four treatments, supplying no BC (corn oil placebo = PL), 30,000 IU/day (BC30), 60,000 IU/day (BC60) and 90,000 IU/day (BC90), all expressed as vitamin A equivalents, and extracted from *Dunaliella salina*. All subjects consumed green and yellow vegetables supplying approximately 25,000-30,000 IU/day BC. After 12 weeks no subject developed skin yellowing on placebo or on BC30 (BC from food and treatment about 60,000 IU/day), 7 out of 9 had some skin yellowing on BC60 (90,000 IU from food plus treatment). All subjects developed skin yellowing on BC90 (120,000 IU from food and treatment). It appears that the threshold for skin yellowing on BC from foods and supplements is above 90,000 IU/day (mean serum BC + S.E.M. 378-43 mcg/dl). Some of the subjects on 90BC (over 100,000 IU/day diet plus supplement) developed occasional pruritus. Standard serum chemistries revealed no toxic effects on any of the treatments.

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THE MODIFIED RELATIVE DOSE RESPONSE (MDR) USING 3,4-DIHYDRO-RETINOL AND ITS APPLICATION TO A POPULATION OF WELL-NOURISHED CHILDREN. Sherry A. Tanumihardjo, Paul C. Koellner and James A. Olson. Iowa State University, Ames, IA 50011.

The relative dose response first proposed by Underwood and her colleagues has proven to be a useful indicator of marginal vitamin A status. We have proposed (J. Nutr. 118: 598-603, 1988) the use of 3,4-dihydroretinol in a similar assay requiring only one blood sample for analysis. In the present experiment, 21 healthy children, ages 4-7, were given a single dose of 3,4-dihydroretinyl acetate (100 mg/kg body weight) in a corn oil solution followed by a 3 oz. serving of ice cream, usually administered in the morning at the child's home. A single blood sample was taken at the McFarland Clinic (Ames, IA) at either 4, 5, 6, 8, 10, or 24 h after the dose. Frozen plasma samples were then extracted and analyzed for dehydroretinol, retinol, retinyl esters, lutein, lycopene, α -carotene and β -carotene using gradient reversed-phase HPLC. The mean ratio of dehydroretinol to retinol plateaued between 4 and 8 h at approximately 0.025 and then fell to a value of 0.006 at 24 h. Only 2 of the 21 children showed ratios >0.03 . These results provide good reference values for healthy midwestern children. The method will now be applied to a population of under-nourished children.

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PLASMA RESPONSES TO ORAL CAROTENE SUPPLEMENTATION IN WELL-NOURISHED GUATEMALAN CHILDREN. H.W. Solomon, J. Bulux, A.F. Lima, J. Quin de Serrano, C. Harrison, L. Kettel, R. Perez, C. Rivera, B.D. Duncan, L.H. Canfield. Departments of Biochemistry, Family and Community Medicine and Pediatrics, University of Arizona, Tucson, AZ 85724, and Center for Studies of Sensory Impairment, Aging and Metabolism (CaSSIAM), Guatemala City, Guatemala, C.A.

Twenty-one healthy children (14 males, 7 females), aged 10 to 14 years consumed 30 mg purified β -carotene (Hoffman-La Roche) with 1 c hot chocolate containing 3 ml vegetable oil. Children consumed a defined diet over the period of the study. Dietary patterns at the beginning of the study were assessed by a food-frequency instrument. Blood samples were obtained at 0, 2, 3, 4, 6, 8, 9 hours from an indwelling catheter and at 24 and 48 hours by venipuncture. In 67% of the subjects, plasma carotene levels increased >5 ng/dl within 8 hours and continued to increase up to 24 hours. Among responders, the maximum increase ranged from 3.2 to 31.1 ng/dl (mean: 21.3 ng/dl). Intakes of both retinol and carotene prior to the study varied widely, but there was no apparent relationship of either of these nutrients in the diet to initial β -carotene levels or plasma response to carotene supplementation.

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THE SITE OF CONVERSION OF ENDOGENOUS ALL-TRANS RETINOID TO 11-CIS RETINOID IN THE BOVINE EYE. W. Shi and J.A. Olson. Dept. of Biochem. & Biophys., Iowa State Univ., Ames, IA 50011.

By use of high-resolution HPLC for the separation of isomeric retinoids, retinal pigment epithelial tissue (RPE) and neural retinal tissue (NR) from pairs of fresh bleached bovine eyes were separately incubated in the dark at either 30°C or 4°C for 90 min. In the RPE, 11-cis retinyl ester (RE), 11-cis retinal oxide (RO), and 11-cis retinol (ROL) increased at 30°C vs 4°C (total $-10.7 \pm 3.5\%$, $n=4$), but all-trans RE, all-trans RO, and all-trans ROL decreased (total $-10 \pm 3.4\%$). In isolated NR, the relative amounts of 11-cis and all-trans retinoids did not significantly change during incubation. Major forms of vitamin A in RPE and NR were RE (70%) and all-trans ROL (60%), respectively. By using modified procedures, we have confirmed reports (Bernstein, Lew & Saudo, Proc Natl Acad Sci 84:1849, 1987; Bridges & Alvarez, Science 236:1678, 1987) that radioactive all-trans ROL is isomerized to 11-cis forms in homogenates of RPE, and to a much smaller degree of NR. In the homogenized bleached bovine eye cup, 11-cis retinal is readily formed from endogenous all-trans ROL. In this case, however, the retinoid pattern of NR, but not of RPE, markedly changes (Landers & Olson, FASEB J. 2:19, 1988). Thus, the RPE seems to be the primary site of 11-cis retinoid formation from all-trans retinoids in the bovine eye. Subsequent transfer of 11-cis retinoids from RPE to NR, however, must be both rapid and highly controlled. Supported by W18-EY 03677.

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RESPONSES OF WEANLING PIGS TO DIETARY LEVELS OF VITAMIN A AND D. R. Blair, B.A. Burton, C.E. Doige, A.C. Halstead and F.E. Newhouse. Depts. of Animal Science and Pathology, University of British Columbia, Vancouver, B.C. V6T 2A2, and University of Saskatchewan, Saskatoon, Sask. S7N 0W0.

Weanling cross-bred pigs (36 or 48) were caged individually and fed diets containing a supplement of vitamin A (Expt.1) or vitamin D3 (Expt. 2) at levels representing 1, 5, 10, 25, 50 and 100 times the NRC (1988) estimated requirements, for 5 weeks. Growth rate, feed intake and feed/gain ratio were not influenced significantly. In Expt. 1 the plasma retinol concentrations were at 5 weeks, respectively, 31.7, 39.4, 43.2, 42.9, 44.4 and 46.3 ng/dl (P 0.05). In Expt. 2 the plasma 25(OH)D3 concentrations were at 5 weeks, respectively, 22.5, 29.5, 35.7, 46.2, 79.9, and 135.3 ng/ml (P 0.001). Histological examination of lung, stomach, kidney, liver and heart indicated no abnormalities, but focal microscopic lesions consistent with osteochondrosis were found in pigs receiving vitamin A at levels over 10 times the requirement. The incidence of osteochondrosis at 3 weeks was, respectively, 0/6, 0/6, 0/6, 0/6, 0/6, and 1/6, and at 5 weeks was, respectively, 0/6, 0/6, 0/6, 0/6, 2/6, 2/6, and 2/6.

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ABSTRACTS

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