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RESEARCH NEWS

Vitamin A, Bones, and Children

A review of: Michaelsson K, Lithell H, Vessby B, Melhus H 2003 Serum retinol levels and the risk of fracture. New Engl J Med 348:287–294

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A RECENT ISSUE of the *New England Journal of Medicine* included an interesting and concerning report linking higher than average vitamin A levels with fractures (1). The study prompts questions about the validity of routine vitamin A supplementation (2).

Karl Michaelsson and colleagues studied 2322 adult men in Sweden (1). They tested vitamin A levels at enrollment (age 49–51 years) and followed the men for 30 years. Fractures were identified in 266 men and were most common in men whose vitamin A levels were in the highest quintile. In fact, having a vitamin A level at or greater than the 99th percentile gave a sevenfold increased risk of fracture when compared to men with lower levels. This new study is similar to previous studies that linked higher fracture rates to hypervitaminosis A.

Retinoic acid, an active metabolite of vitamin A, prompts osteoclastic activity and bone resorption. Hypervitaminosis A would be expected to increase circulating levels of retinoic acid and thereby lead to bone resorption and more fractures.

How does this relate to children? Clearly, vitamin A insufficiency is common in many areas of the world, accounts for many cases of blindness, and is linked to high mortality (3). Community-based supplementation of vitamin A yields decreased mortality, and, in patients with measles, supplementation decreases morbidity (3). Dietary intake of vitamin A is associated with reductions in mortality, diarrheal and respiratory infections, and stunting (4). Even though there is inconsistency in results of studies of pharmacologic vitamin A supplementation (4), limitation of dietary vitamin A intake in developing countries could have markedly negative consequences on many children.

In fact, there is also evidence that low vitamin A intake is associated with decreased bone density, at least in older adults (5). As pointed out by Michaelsson's study (1), our goal should be to provide appropriate vitamin A intake for adults. Similarly, we should continue to strive to provide adequate vitamin A for children, being careful to avoid intakes that are either too high or too low. Michaelsson's report should heighten our efforts to provide appropriate vitamin A supplementation to children and should not hinder ongoing supplementation for children in areas of the world where vitamin A deficiency is common.

1. Michaelsson K, Lithell H, Vessby B, Melhus H 2003 Serum retinol levels and the risk of fracture. New Engl J Med 348:287–294
2. Lips P 2003 Hypervitaminosis A and fractures (editorial). New Engl J Med 348:347–349
3. Underwood BA, Arthur P 1996 The contribution of vitamin A to public health. FASEB J 10:1040–1048
4. Villamor E, Fawzi WW 2000 Vitamin A supplementation: implications for morbidity and mortality in children. J Infect Dis 182(Suppl 1):S122–S133
5. Promislow JH, Goodman-Gruen D, Slymen DJ, Barrett-Connor E 2002 Retinol intake and bone mineral density in the elderly: the Rancho Bernardo study. J Bone Miner Res 17:1349–1358

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Sudden Infant Death Syndrome Is Preceded by Hypoxia

A review of: Jones KL, Krous HF, Nadeau J, Blackbourne B, Zielke HR, Gozal D 2003 Vascular endothelial growth factor in the cerebrospinal fluid of infants who died of sudden infant death syndrome: evidence for antecedent hypoxia. Pediatrics 111:358–363

OLA DIDRIK SAUGSTAD
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NAEYE SHOWED IN a large autopsy series in 1980 that infants who succumbed to sudden infant death syndrome (SIDS) had morphological signs of antecedent hypoxia in several organs (1). Among the most important findings were brain stem gliosis, also described by Takashima *et al.* two years earlier (2), and confirmed by Kinney *et al.* (3), and Valdes-Dapena *et al.* (4). Since brainstem astrogliosis takes several days to develop, a search for biochemical hypoxia markers was initiated. The first biochemical evidence was demonstration of elevated hypoxanthine in vitreous humor in approximately 80% of SIDS cases (5, 6).