



# THE SUPPLEMENT

VOLUME 3, ISSUE 1 JANUARY 2005



## VITAMIN A AND CYSTIC FIBROSIS

Vitamin A exists in various forms--preformed and its precursors, the carotenoids. Vitamin A's role in vision is well documented. It is also essential for many other body functions including growth, immunocompetence, and bone and tooth development. In CF, the historical focus was on overt deficiency manifestations. Currently, the trend is to investigate the more subtle roles of vitamin A in overall health, including liver and lung integrity. The independent roles of the carotenoids in CF is an emerging research area. For a review of vitamin A the reader is directed to a current advanced nutrition text and the chapter on vitamin A in the DRIs.

### FEATURED PAPERS:

**Longitudinal analysis shows serum carotenoid concentrations are low in children with cystic fibrosis. Kawchak DA, Sowell AL, Hofley PM, Zemel BS, Scanlin TF, Stallings VA. J Am Dietet Assoc 1999;99:1569-72.**

**Objective:** To compare serum concentrations of 5 carotenoid compounds and retinol; examine the relationship between serum carotenoid concentrations and fat absorption; and document dietary intake of vitamin A and carotenoids. **Subjects:** 24 PI children, 12 female, mean age at start of research 7.8yrs $\pm$ 1.4 yrs, range 6 to 10 yrs, all had mild disease. **Design:** Three year longitudinal study with children evaluated 4 times at yearly intervals. **Results:** Preformed vitamin A intake and serum levels were within normal limits. Food carotenoid intake exceeded NHANES III values, yet serum levels were low. Low carotenoid levels usually were found with fat malabsorption. **Conclusions:** Further research is needed regarding carotenoids and CF.

**Faecal elastase-1 and fat-soluble vitamin profiles in patients with cystic fibrosis in Western Norway. Dorlochter L, Aksnes L, FlugeG. Eur J Nutr. 41:148-52, 2002.**

**Objective:** To correlate pancreatic function with fat-soluble vitamin serum levels; compare fat-soluble levels in PI vs. PS patients; and assess efficacy of fat-soluble vitamin supplementation. **Subjects:** 35 patients, 24 PI, 16 female, mean age 12.1 $\pm$ 8.9 yrs, range 2-40 yrs. **Design:** Eight year study with some subjects starting at diagnosis. **Results:** No difference in fat-soluble vitamin serum levels in PI or PS patients when on appropriate vitamin supplements. **Conclusions:** Fat-soluble vitamins given in appropriate doses with pancreatic enzymes for PI patients, resulted in normal serum retinol levels.

**Lutein, zeaxanthin, macular pigment, and visual function in adult cystic fibrosis patients. Schupp C, Olano-Martin E, Gerth C, Morrissey BM, Cross CE, Werner JS. Am J Clin Nutr 2004;79:1045-52.**

**Objective:** To determine plasma carotenoid levels; assess retinal health and visual function. **Subjects:** 10 adult PI, CF patients, 9 male. Mean age 31.2 yrs  $\pm$ 10 yrs, range 21-47 yrs and 10 age and gender matched controls. **Design:** Cross-sectional study of adults. **Results:** Serum lutein and zeaxanthin and macular pigment density significantly reduced in CF patients; no significant difference found in visual function between CF and controls. **Conclusions:** Since clinical ocular changes may not occur until after 50 years of age, authors recommended a larger study sample, followed longitudinally.

### SPECIAL POINTS OF INTEREST:

- The independent roles of the carotenoids in CF is an emerging research area.
- One study found that fat-soluble vitamins given in appropriate doses with pancreatic enzymes for PI patients, resulted in normal serum retinol levels.

Volume 3, Issue 1:  
Author: Suzanne H. Michel, MPH, RD, LDN  
Editor: Donna H. Mueller, PhD, RD, FADA, LDN

## REVIEW

In developing countries, morbidity and mortality is linked to vitamin A deficiency. In the United States, the American Academy of Pediatrics recommends vitamin A supplementation for all children hospitalized with measles. (1) For persons who have CF, there is long-standing recognition of vitamin A's importance. (2) Prior to heightened attention to nutrition and the availability of enteric-coated enzymes, vitamin A deficiency was common, (3,4).

Infants diagnosed through newborn screening may be vitamin A deficient (5) Most times, the levels reach normal when the babies are treated with appropriate enzyme and vitamin supplements (6). With expert nutrition management, normal serum retinol levels were reported in the featured paper by Dorlechter as well as others (7). However, vitamin A deficiency may occur in PS patients and in PI patients treated with enzymes and vitamin supplements. (8, 9)

This may be due to any number of factors including: 1. Maldigestion and malabsorption; 2. Impaired lymph and blood vitamin A circulation; 3. Decreased mobilization of liver stores;(10) 4. Abnormal function of retinol binding protein and other transport proteins; (11) 5.

Increased fecal loss; (12) 6. Liver disease; (13) 7. Increased infection and inflammation; (11) and 8. Compromised overall nutritional status.

Vitamin A deficiency may result in night blindness (14), a particular concern for patients who drive. As noted above (Schupp) and by others (15), subtle changes in eye health are more difficult to document and may not become evident until the patient is well into adulthood.

Limited studies are available describing the use of beta-carotene as a source of retinol in CF. (16) As demonstrated by Kawchak and others, (16,17) low plasma beta-carotene levels have been found in CF, even with adequate food intake.

**“ . . . VITAMIN A DEFICIENCY MAY OCCUR IN PS PATIENTS AND IN PI PATIENTS TREATED WITH ENZYMES AND VITAMIN SUPPLEMENTS.”**

## CLINICAL APPLICATIONS

The CFF (18) recommends an intake of 1,500 to 10,000 IU; the range is age dependent. In clinical practice each patient's dosage can be variable (19). Annual evaluation of blood retinol level should be routine. (9, 18)

Continuous assessment of overall nutrition status is imperative. This involves evaluation of enzyme use and dietary intake from food and vitamins, as well as from proprietary (20) and home-made supplements. Nutrients impacting vitamin A status are calories, protein, fat, vitamins E and K, iron, and zinc. Alcohol consumption must be considered. It is important to confirm that the patient is in concordance with recommendations. When vitamin A deficiency is refractory to standard intervention, supplements of individual nutrients, such as zinc, may be helpful. (18)

Beta-carotene contributes to vitamin A nutrition, and along with other carotenoids, is important for overall

health. RDs educate patients to include brightly colored fruits and vegetables in their usual diet as part of a high caloric intake. (21)

**“THE RD PLAYS A PIVOTAL ROLE IN HELPING PATIENTS REACH OPTIMAL VITAMIN A HEALTH BY MONITORING NUTRITIONAL AND CLINICAL STATUS, AND BY TEACHING A BALANCED FOOD INTAKE COUPLED WITH VITAMIN SUPPLEMENT AND ENZYME USE.”**

Although in patients with CF more attention is paid to retinol deficiency, in the **non-CF** population there is evidence that excessive retinol intake can be detrimental to the liver (22) bone (23), and developing fetus (24). To date there are no published reports of such findings among persons who have CF. Nevertheless, it is suggested that serum retinol levels be maintained within normal limits. (19, 25) Laboratory assessment of retinol level is best undertaken while the patient is healthy. Retinol levels may be depressed during periods of CF exacerbation. (11)

The RD plays a pivotal role in helping patients reach optimal vitamin A health by monitoring nutritional and clinical status, and by teaching a balanced food intake coupled with vitamin supplement and enzyme use.

## REFERENCES

1. American Academy of Pediatrics Committee on Infectious Diseases. Vitamin A treatment of measles. *N Engl J Med.* 91:1014-5, 1993.
2. Blackfan KD, Wolbach SB. Vitamin A deficiency in infants: a clinical and pathological study. *J Pediatr* 3:679-706, 1933.
3. Underwood BA, et al. Blood and liver concentrations of vitamins A and E in children with cystic fibrosis of the pancreas. *Pediatr Res.* 6:26-31, 1972
4. Palin D, Underwood BA, et al. The effect of oral zinc supplementation on plasma levels of vitamin A and retinol-binding protein in cystic fibrosis. *Am J Clin Nutr.* 32:1253-9, 1979.
5. Sokol RJ, Reardon MC, et al. Fat-soluble-vitamin status during the first year of life in infants with cystic fibrosis identified by screening of newborns. *Am J Clin Nutr.* 50:1064-71, 1989.
6. Feranchak AP, Sontag MK, et al. Prospective, long-term study of fat-soluble vitamin status in children with cystic fibrosis identified by newborn screen. *J Pediatr.* 135:601-610, 1999.
7. Ansari EA, Sahni K, et al. Ocular signs and symptoms and vitamin A status in patients with cystic fibrosis treated with daily vitamin A supplements. *Br J Ophthalmol.* 83:688-91, 1999.
8. Lancellotti L, D'Orazio C, et al. Deficiency of vitamins E and A in cystic fibrosis is independent of pancreatic function and current enzyme and vitamin supplementation. *Eur J Pediatr.* 155:281-85, 1996.
9. Jaffe A, Buchdahl R, et al. Are annual blood tests in preschool cystic fibrosis patients worthwhile? *Arch Dis Child.* 87:518-21, 2002.
10. Benabdeslam H, Garcia I, et al. Biochemical assessment of the nutritional status of cystic fibrosis patients treated with pancreatic enzyme extracts. *Am J Clin Nutr.* 67:912-8, 1998.
11. Duggan C, Colin AA, et al. Vitamin A status in acute exacerbations of cystic fibrosis. *Am J Clin Nutr* 64:635-9, 1996.
12. Ahmed F, Ellis J, et al. Excessive faecal losses of vitamin A (retinol) in cystic fibrosis. *Arch Dis in Childhood.* 65:589-93, 1990.
13. Lindblad A, Diczfalusy U, et al. Vitamin A concentration in the liver decreases with age in patients with cystic fibrosis. *J Pediatr Gastroenterol Nutr.* 24:264-270, 1997.
14. Huet F, Semama DM, et al. Vitamin A deficiency and nocturnal vision in teenagers with cystic fibrosis. *Eur J Pediatr.* 156:949-51, 1997.
15. Morkeberg JC, Edmund C, et al. Ocular findings in cystic fibrosis patients receiving vitamin A supplementation. *Graefe's Arch Clin Exp Ophthalmol.* 233:709-13, 1995.
16. Winkhofer-Roob BM, van't Hof MA, et al. Response to oral beta-carotene supplementation in patients with cystic fibrosis: a 16-month follow-up study. *Acta Paediatr.* 84:1132-6, 1995.
17. Renner S, Rath R, et al. Effects of beta-carotene supplementation for six months on clinical and laboratory parameters in patients with cystic fibrosis. *Thorax.* 56:48-52, 2001.
18. Borowitz D, Baker RD, Stallings V. Consensus report on nutrition for pediatric patients with cystic fibrosis. *J Pediatr Gastro Nutr.* 35:246-259, 2002.
19. James DR, Own G, Campbell IA, Goodchild MC. Vitamin A absorption in cystic fibrosis: risk of hypervitaminosis A. *Gut.* 33:707-10, 1992.
20. Bhall K, Ennis DM, Ennis ED. Hypercalcemia caused by iatrogenic hypervitaminosis A. *J Am Diet Assoc.* 105:119-21, 2005.
21. Wood LG, Fitzgerald DA, et al. Increased plasma fatty acid concentrations after respiratory exacerbations are associated with elevated oxidative stress in cystic fibrosis patients. *Am J Clin Nutr.* 75:668-75, 2002.
22. Jorens PG, Michielsen PP, Pelckmans PA, et al. Vitamin A abuse: development of cirrhosis despite cessation of vitamin A. A six-year clinical and histopathologic follow-up. *Liver.* 12:381-6, 1992.
23. Michaelsson K, Lithell H, Vessby B, et al. Serum retinol levels and the risk of fracture. *N Engl J Med.* 348:287-94, 2003.
24. Dietary Reference Intakes for Vitamin A, 2001. Food and Nutrition Board, Institute of Medicine. National Academy Press, page 139.
25. Sinaasappel M, Stern M, et al. Nutrition in patients with cystic fibrosis: a European Consensus. *J CF.* 1:51-75, 2002.



**EURAND PHARMACEUTICALS, INC.**

790 Township Line Road  
Suite 250  
Yardley, PA 19067

Phone: 267-759-9400  
E-mail: [newsletterinfo@eurand.com](mailto:newsletterinfo@eurand.com)

---

**Visit our Web Site**  
**[www.eurand.com](http://www.eurand.com)**

---

**ABOUT EURAND**

We are a specialty pharmaceutical company that develops, manufactures and commercializes enhanced pharmaceutical and biopharmaceutical products using our proprietary drug formulation technologies. We are dedicated to the continued development and commercialization of breakthrough products that better satisfy patients' needs. Our research efforts are focused on the development of treatment options with enhanced efficacy, superior safety and convenient dosing. We have a pipeline of products in development for ourselves and our co-development collaborators.

The Supplement is an educational service provided by [Eurand Pharmaceuticals, Inc.](http://www.eurand.com) If you would like to be added or removed from our mailing list, please email us at [newsletterinfo@eurand.com](mailto:newsletterinfo@eurand.com)

The information in this publication is presented for educational and guidance purposes only. It should not be used as the basis for any medical diagnosis, prognosis or treatment plan. Anyone seeking medical advice, diagnosis or treatment should consult a qualified medical doctor. We are not responsible for any loss or damage that you, your beneficiaries or your estate may suffer, as reliance on our information is not reasonable for all the forgoing reasons. Please direct any inquiries regarding the same to:

[newsletterinfo@eurand.com](mailto:newsletterinfo@eurand.com)

[Eurand Pharmaceuticals, Inc.](http://www.eurand.com), © 2008 All rights reserved.

Printed in USA NTSCF 1/05