



**UPDATE ON RESEARCH FOR RP  
TREATMENT: VITAMIN A PALAMITATE,  
OMEGA-3-RICH FISH AND LUTEIN**

# VITAMIN A PALMITATE / OMEGA-3-RICH FISH / LUTEIN

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## INTRODUCTION

Foundation-funded clinical research studies conducted by Dr. Eliot Berson and his co-workers at the Harvard Medical School, Massachusetts Eye and Ear Infirmary, demonstrated that the combined treatment regimen of vitamin A palmitate, oily fish and lutein may provide an additional 20 years of useful vision for people who were between 18 and 60 years of age with typical forms of retinitis pigmentosa (RP) or Usher syndrome types 2 or 3. These participants also began the study with best-corrected visual acuity of 20/100 or better.

This document is an update to the information on the treatment regimen previously provided by the Foundation Fighting Blindness.

Dr. Berson's recommended treatment regimen is not appropriate for everyone with a retinal disease, and the decision to take it should only be made between the patient and his or her doctor.

## COMPONENTS OF THE TREATMENT REGIMEN

- 1) Daily vitamin A palmitate supplementation (15,000 IU)
- 2) Weekly consumption of one to two 3-ounce servings of omega-3 rich oily fish of which docosahexaenoic acid (DHA) is a major component (e.g., salmon, tuna, mackerel, herring, sardines).

Individuals who cannot eat oily fish should take one DHA 200 mg gelcap daily.

- 3) Daily lutein supplementation (12 mg)

## DISEASES STUDIED IN DR. BERSON'S CLINICAL RESEARCH

Dr. Berson's clinical study focused on people who were 18 to 60 years of age and had one of the following diseases: typical autosomal recessive RP; autosomal dominant RP; X-linked RP; isolate RP (i.e., no family history); Usher syndrome type 2; and Usher syndrome type 3, with best-corrected visual acuity of 20/100 or better at the start of the study.

Dr. Berson believes that all adults with the above-mentioned forms of retinal disease can benefit from the treatment regimen. However, since the defective gene (genotype) for all of the participants in his study were not known, Dr. Berson and his co-workers are conducting additional research to determine if there are people with particular genotypes who respond to the treatment regimen better than others.

## DISEASES NOT STUDIED IN DR. BERSON'S CLINICAL RESEARCH

The treatment regimen was not studied in people with choroideremia, retinoschisis, Bardet-Biedl syndrome, Usher syndrome type 1B, Leber congenital amaurosis, other forms of retinal degeneration that aren't RP and forms of RP that are considered atypical.

## DISEASES FOR WHICH THE TREATMENT COULD BE HARMFUL

Laboratory research suggests that the treatment regimen may be harmful to people with Stargardt disease, cone-rod dystrophy, Best disease and any retinal disease caused by mutations in the gene *Abca4*.

## IMPORTANT GUIDELINES FROM DR. BERSON

Patients should consult with a doctor before starting this regimen, as high doses of vitamin A (i.e., 25,000 IU/day or higher) can be toxic to the liver. Patients should have both a fasting serum vitamin A test and a liver function profile test before starting the regimen. While on the regimen, patients should have both tests at least once a year. It is important that patients do not take vitamin A palmitate if liver function is abnormal. For patients with a normal liver function, vitamin A palmitate 15,000 IU/day is considered safe, and no toxic effects have been reported for those taking this dose for 25 years.

If patients already have a diet high in vitamin A, or take other supplements containing high levels of vitamin A, their doctor should adjust the dose appropriately. Further recommendations on this are given below.

Only vitamin A palmitate should be taken. Other forms of vitamin A, including beta carotene, are not effective substitutes.

Patients should talk to their doctor about consuming oily fish, because in some people it can raise cholesterol levels.

Patients should not exceed the recommended intakes of vitamin A palmitate, oily fish (or DHA) and lutein supplements, because higher doses have not been shown to provide greater benefit. In the case of oily fish, excessive oily fish (e.g., salmon steaks daily) could result in the release of too much vitamin A into the retina, having an adverse effect on vision over the long-term.

People with RP should not take high doses of vitamin E (400 IU per day or more), because it lowers serum vitamin A levels and has been reported to accelerate the course of RP.

Adults who consume alcohol heavily should not take this regimen. Adults following this regimen should limit their alcohol intake to no more than two alcoholic beverages per day.

Women who are pregnant or planning to be pregnant are advised not to take vitamin A palmitate 15,000 IU per day because of the increased risk of birth defects.

Women and men over age 49 with RP have a slight (0.5%-1%) increased risk of hip fracture on this dose of vitamin A. Patients with RP in this age group should have their bone density measured every 1-2 years. If osteoporosis develops, your doctor may prescribe additional medication. Depending on the severity of the RP and the severity of the osteoporosis, your physician may instruct you to discontinue this regimen.

People who have had renal transplants should not take vitamin A palmitate, because the transplanted kidneys may reabsorb too much vitamin A, raising the possibility of developing toxicity.

People taking a type of medication called tetracyclines, which is taken for many conditions, including chronic acne, should not take high-dose vitamin A palmitate, because of the increased risk of raising intracranial pressure. Such individuals should consult with their doctor about alternative solutions for their acne if they wish to use the vitamin A palmitate regimen.

Lutein supplementation is not advised for current smokers. Evidence exists that this supplement will increase the risk of lung cancer over the long-term among smokers.

## SUMMARIES OF DR. BERSON'S CLINICAL RESEARCH

**Vitamin A palmitate supplementation:** In a research paper published in the June 1993 issue of the *Archives of Ophthalmology*, Dr. Berson and his co-workers reported that patients with RP and Usher syndrome types 2 and 3 taking vitamin A palmitate had, on average, a 20 percent annual slower loss of retinal function, as measured by an electroretinogram (ERG), than those not taking the supplement.

Reference: Berson, E.L., B. Rosner, M.A. Sandberg, K.C. Hayes, B.W. Nicholson, C. Weigel-DiFranco and

W. Willett (1993). "A randomized trial of vitamin A and vitamin E supplementation for retinitis pigmentosa," *Archives of Ophthalmology* 111(6): 761-72.

**Adding oily fish consumption to vitamin A palmitate supplementation:** In a research paper published in the June 2012 issue of the *Archives of Ophthalmology*, Dr. Berson and his co-workers reported that patients supplementing with vitamin A palmitate and consuming one to two 3-ounce servings of oily fish per week had, on average, a 40 percent annual slower loss in visual acuity than those supplementing with vitamin A palmitate alone.

Reference: Berson, E.L., B. Rosner, M.A. Sandberg, C. Weigel-DiFranco and W.C. Willett (2012). "Omega-3 intake and visual acuity in patients with retinitis pigmentosa receiving Vitamin A," *Archives of Ophthalmology* 130: 708-711.

**Benefit of lutein for those taking vitamin A and consuming oily fish:** In a research paper published in the April 2010 issue of the *Archives of Ophthalmology*, Dr. Berson and his co-workers reported that adding lutein to the vitamin A palmitate and oily fish regimen conferred the added benefit of saving, on average, midperipheral visual sensitivity by 2.7 percent per year. Lutein supplementation, on average, slowed midperipheral field loss by as much as 10 years among adults on vitamin A palmitate.

Reference: Berson, E.L., B. Rosner, M.A. Sandberg, C. Weigel-DiFranco, R.J. Brockhurst, K.C. Hayes, E.J. Johnson, E.J. Anderson, C.A. Johnson, A.R. Gaudio,

W.C. Willett and E.J. Schaefer (2010). "Clinical trial of lutein in patients with retinitis pigmentosa receiving vitamin A," *Archives of Ophthalmology* 128(4): 403-11.

**Medical Disclaimer:** Physicians differ in their approach to incorporating research results into their clinical practice. You should always consult with and be guided by your physician's advice when considering treatment based on research results. This information is provided for information purposes only. The Foundation Fighting Blindness takes no position on the efficacy or safety of this treatment regimen. In particular, nothing herein should be construed as a recommendation that the reader should undertake this treatment regimen.

## ANSWERS TO FREQUENTLY ASKED QUESTIONS

### **Do I need to take all three components of the recommended treatment regimen to get some benefit for my vision?**

Dr. Berson and his co-workers showed that vitamin A palmitate 15,000 IU/day alone would, on average, slow visual loss in adults with typical RP. Their evaluations of oily fish consumption and lutein were among people already taking vitamin A palmitate. Their research did not evaluate the effect of oily fish consumption alone or lutein supplementation alone. Based on their research, you can take vitamin A palmitate alone to get some benefit of slowing the course of disease. But whether there is any visual benefit in eating oily fish alone or taking lutein alone is not known.

### **Will I know if the treatment is working or not?**

It is unlikely that you will notice an improvement in your vision, because the regimen has been shown to slow your loss of vision rather than improve or restore your vision. The treatment gives you a better chance of retaining more vision in the long term; the projected benefit is up to 20 additional years of visual acuity and central visual field for the average patient who starts the regimen of vitamin A palmitate 15,000 IU/day and one to two 3-ounce servings of oily fish per week by age 40. The disease process continues but at a slower rate. The treatment is not a cure.

### **Why do I need to take vitamin A palmitate under a doctor's supervision?**

A physician, preferably an ophthalmologist, will need to order blood tests to measure your fasting levels of vitamin A and to assess your liver function before starting treatment. These tests should be taken each year while under the regimen. These tests are needed to ensure that you don't have a pre-existing medical condition that would prevent you from taking this treatment. Liver toxicity is a potential complication of high daily doses of vitamin A palmitate, so blood tests to assess your liver function should be performed by your doctor annually. As reported in the vitamin A palmitate study and subsequently, no significant acute or chronic toxicity has been found in adults taking this dose of vitamin A palmitate.

Reference: Sibulesky, L., Hayes, K.C., Pronczuk, A., Weigel-DiFranco, C., Rosner, B., Berson, E.L. (1999) "Safety of less than 7,500 RE/day (25,000 IU/day) of

vitamin A in adults with retinitis pigmentosa," *Amer J Clin Nutr* 69:656-663.

### **What if I take a multivitamin that already has vitamin A?**

Dr. Berson advises that if an adult with RP is taking a supplement of 15,000 IU/day of vitamin A palmitate, he or she can also take one multivitamin/day as long as it contains no more than 5,000 IU of vitamin A and 30 IU of vitamin E. If the patient misses vitamin A palmitate on a given day, he or she should not take two doses the next day.

### **Who shouldn't take vitamin A palmitate, lutein, and/or consume oily fish?**

Dr. Berson's research studies included people who were 18 to 60 years of age with typical autosomal recessive RP, autosomal dominant RP, X-linked RP, isolate RP (i.e., no family history) and Usher syndrome types 2 and 3. At the start of the study, the participants also had best-corrected visual acuity of 20/100 or better. This is the group clinical studies have shown can benefit.

Laboratory research suggests that the treatment regimen may be harmful to people with Stargardt disease, cone-rod dystrophy, Best disease and any retinal disease caused by mutations in the gene *Abca4*.

People who have abnormal fasting serum vitamin A or liver function profile should not take vitamin A palmitate.

People who consume alcohol heavily should not take this regimen. Adults on this regimen should weigh over 90 pounds and limit their alcohol intake to no more than two alcoholic beverages per day.

Women who are pregnant or planning to be pregnant are advised not to take vitamin A palmitate 15,000 IU per day because of the increased risk of birth defects.

Women and men over age 49 with RP have a slight (0.5%-1%) increased risk of hip fracture on this dose of vitamin A. Patients with RP in this age group should have their bone density measured every 1-2 years. If osteoporosis develops, your doctor may prescribe additional medication. Depending on the severity of the RP and the severity of the osteoporosis, your physician may instruct you to discontinue this regimen.

People who have had renal transplants should not take vitamin A palmitate, because the transplanted kidneys may reabsorb too much vitamin A, raising the possibility of developing toxicity.

People taking a type of medication called tetracyclines, which is taken for many conditions, including chronic acne, should not take high-dose vitamin A palmitate, because of the increased risk of raising intracranial pressure. Such individuals should consult with their doctor about alternative solutions for their acne if they wish to use the vitamin A palmitate regimen.

People who smoke should not take lutein, because some studies have shown that lutein can further increase lung cancer risk in smokers.

### **Can my child take vitamin A palmitate and lutein, and eat oily fish?**

Dr. Berson's published clinical research studies on the safety and efficacy of vitamin A palmitate, oily fish and lutein for typical RP and Usher syndrome types 2 and 3 did not include patients under the age of 18.

The impact of chronic, high doses of vitamin A in young people is not known, but children are particularly sensitive to vitamin A. If your physician is considering the regimen for a patient under the age of 18, an appropriately reduced dose of vitamin A palmitate should be used. Your physician should also be aware of rare, but serious complications that can occur in children using vitamin A, such as pseudotumor cerebri. This syndrome includes headache, nausea and vomiting, as well as pulsatile tinnitus, double vision and other visual symptoms. If untreated, it may lead to swelling of the optic disc in the eye, which can progress to vision loss.

### **Does the vitamin A have to be the palmitate form?**

Yes. Vitamin A palmitate was the form of vitamin A used in the study. Other forms of vitamin A, including beta carotene, are not substitutes for the palmitate form.

### **What if I don't like oily fish or am allergic to it?**

If a patient is allergic to fish or simply won't eat it, they are advised to take one 200mg DHA gelcap per day.

### **What if I eat more fish or take more DHA than recommended?**

Excessive intake of oily fish or DHA is to be avoided. Preliminary evidence suggests that too much oily fish could result in too much vitamin A being released in the retina with a potential for hastening the loss of cone function, and vision, over the long term.

### **I'm not sure what kind of RP or Usher syndrome I have – can I still take vitamin A palmitate and lutein, and eat oily fish?**

The decision to take the treatment regimen should be made between you and your doctor. If your doctor is uncertain as to whether your disease is one of the treatment-appropriate diseases listed in this document, you should not take the regimen. Your doctor may recommend a genetic test or additional examinations to confirm your diagnosis and your eligibility for the treatment.

### **I want to take vitamin A palmitate, but my doctor doesn't think it works or thinks it is unsafe – what should I do?**

Please refer your doctor to the published literature and these guidelines. No published studies have revealed any adverse effect of vitamin A palmitate at the recommended levels on retinal function in adults with RP. Moreover, no systemic toxic effects of vitamin A palmitate have been reported among adults taking 15,000 IU/day for 4-6 years in 3 clinical trials (*Archives of Ophthalmology*, 1993, 2004 and 2010). Some adult patients have taken this dose of vitamin A palmitate since 1984, and no significant toxic side effects (including no liver toxicity) have been reported as of June 2012.

Additionally, in June of 1993, following publication of the original trial, the National Eye Institute mailed 40,000 letters nationwide to practicing ophthalmologists and optometrists endorsing the use of vitamin A palmitate 15,000 IU/day for adults with typical forms of RP. The National Eye Institute reaffirmed this recommendation in 2008 (NEI Statement: "Update on Vitamin A as a Treatment for Retinitis Pigmentosa, Optometry and Vision Science" 85(9):E790-E791).

Many practicing ophthalmologists are aware that vitamin A palmitate is used to treat RP. This document can guide your physician to the relevant literature.

If you cannot find a doctor in your region, please contact the Foundation Fighting Blindness to seek an appropriate referral.

#### **Where can I buy vitamin A palmitate?**

The high dose capsules of 15,000 IU vitamin A palmitate are not always available in local stores but can be purchased by mail order from several U.S. suppliers. An Internet search using terms like "15,000 IU vitamin a palmitate" should help you identify sources.

#### **What brand of lutein should I take?**

Lutein is usually available in local stores, and any reputable brand should be appropriate. Adults should take 12 mg (e.g., two 6 mg pills) per day.

#### **What brand of DHA should I take?**

In his study Dr. Berson used the brand Neuromins, which does not contain the fatty acid

eicosapentaenoic acid (EPA) or any additional vitamins. Any equivalent brand should be appropriate.

#### **Where can I get more information?**

Visit [www.FightingBlindness.org](http://www.FightingBlindness.org) or call 1-800-683-5555.