ARMD
From Spinach to Injection

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Risk Factors *determined by the Mayo Clinic*

- **Age.** Your risk of macular degeneration increases as you age, especially after age 50. Macular degeneration is most common in people older than 65.
- **Family history of macular degeneration.** If someone in your family had macular degeneration, you're more likely to develop macular degeneration.
- **Race.** Macular degeneration is more common in whites (Caucasians) than it is in other races.
- **Smoking.** Smoking cigarettes increases your risk of macular degeneration.
- **Obesity.** Being severely overweight increases the chance that early or intermediate macular degeneration will progress to the more severe form of the disease.
- **Diet.** A diet that includes few fruits and vegetables may increase the risk of macular degeneration.
- **High blood pressure.** Diseases that affect the circulatory system, such as high blood pressure or high cholesterol, may increase the risk of macular degeneration.
- **Inflammation.** Your immune system can cause swelling of your body tissues, which may increase the risk of macular degeneration.
- **Cardiovascular disease.** If you have had diseases that affected your heart and blood vessels (cardiovascular disease), you may be at higher risk of macular degeneration

ARMD genetics

– Alternate complement pathway
– ARMS2/HTRA1
– HDL cholesterol pathway
– Extracellular matrix
– Angiogenesis pathway
– Vitamin D pathway

Hippocrates

"He who does not know food, how can he understand the diseases of man?"

Our body was designed to absorb nutrients the old fashioned way…by eating natural foods rich in antioxidants. Locally grown, organic fruits and vegetables contain the essential vitamins and nutrients necessary for optimal health.

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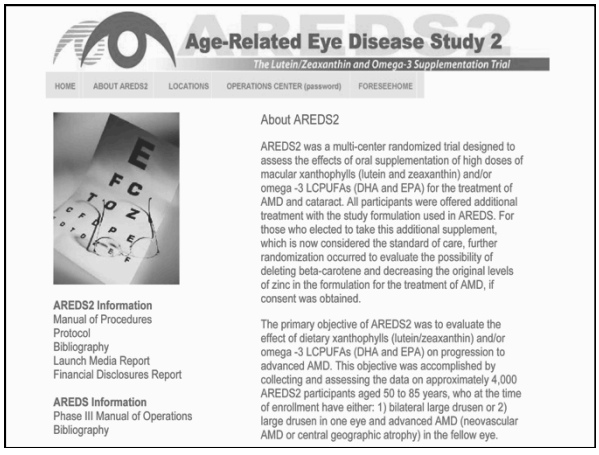
Design Paper

The Age-Related Eye Disease Study (AREDS): Design Implications AREDS Report No. 1

The Age-Related Eye Disease Study Research Group[1]

ABSTRACT: The Age-Related Eye Disease Study (AREDS) was initially conceived as a long-term multicenter, prospective study of the clinical course of age-related macular degeneration (AMD) and age-related cataract. Data on progression rates and risk factors from the study will increase understanding of the clinical course of both conditions, generate hypotheses about etiology, and aid in the design of clinical trials of potential interventions. In addition to collecting natural history data, AREDS includes a clinical trial of high-dose vitamin and mineral supplements for AMD and a clinical trial of high-dose vitamin supplements for cataract. The clinical trials were initiated largely because of the widespread public use in the United States of commercially available pharmacologic doses of vitamins and minerals to treat these two eye conditions and the absence of definitive studies on the safety and efficacy of their use. Important design issues for the clinical trials include: defining cataract and AMD, estimating event rates, determining the type and dosage of vitamins and minerals to be tested for each condition, and identifying the parameters necessary for monitoring safety and efficacy. This paper describes the AREDS design, including the study rationale and operational structure, and the approach adopted to combine, for two diseases, clinical trials with a natural history study. *Control Clin Trials* 1999;20:573–600 © Elsevier Science Inc. 1999



AREDS2

Age-Related Eye Disease Study 2

The Lutein/Zeaxanthin and Omega-3 Supplementation Trial

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About AREDS2

AREDS2 was a multi-center randomized trial designed to assess the effects of oral supplementation of high doses of macular xanthophylls (lutein and zeaxanthin) and/or omega -3 LCPUFAs (DHA and EPA) for the treatment of AMD and cataract. All participants were offered additional treatment with the study formulation used in AREDS. For those who elected to take this additional supplement, which is now considered the standard of care, further randomization occurred to evaluate the possibility of deleting beta-carotene and decreasing the original levels of zinc in the formulation for the treatment of AMD, if consent was obtained.

The primary objective of AREDS2 was to evaluate the effect of dietary xanthophylls (lutein/zeaxanthin) and/or omega -3 LCPUFAs (DHA and EPA) on progression to advanced AMD. This objective was accomplished by collecting and assessing the data on approximately 4,000 AREDS2 participants aged 50 to 85 years, who at the time of enrollment have either: 1) bilateral large drusen or 2) large drusen in one eye and advanced AMD (neovascular AMD or central geographic atrophy) in the fellow eye.

AREDS2 Information
Manual of Procedures
Protocol
Bibliography
Launch Media Report
Financial Disclosures Report

AREDS Information
Phase III Manual of Operations
Bibliography

AREDS 2

AREDS 2 is a multi-center randomized trial designed to assess the effects of oral supplementation of high doses of macular xanthophylls (lutein and zeaxanthin) and/or omega -3 LCPUFAs (DHA and EPA) for the treatment of AMD and cataract. All participants will be offered additional treatment with the study formulation used in AREDS. For those who elect to take this additional supplement, which is now considered the standard of care, further randomization may occur to evaluate the possibility of deleting beta-carotene and decreasing the original levels of zinc in the formulation for the treatment of AMD, if consent is obtained.

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AREDS 2

The primary objective of AREDS 2 is to evaluate the effect of dietary xanthophylls (lutein/zeaxanthin) and/or omega -3 LCPUFAs (DHA and EPA) on progression to advanced AMD. This objective will be accomplished by collecting and assessing the data on approximately 4,000 AREDS 2 participants aged 50 to 85 years, who at the time of enrollment have either:

1. bilateral large drusen or
2. large drusen in one eye and advanced AMD (neovascular AMD or central geographic atrophy) in the fellow eye.

The objectives of AREDS 2 are to:

Study the effects of high supplemental doses of the dietary xanthophylls (lutein and zeaxanthin) and omega -3 LCPUFAs (DHA and EPA) on the development of advanced AMD.

Study the effects of these supplements on cataract and moderate vision loss (doubling of the visual angle or the loss of 15 or more letters on the ETDRS chart).

Study the effects of eliminating beta-carotene in the original AREDS formulation on the development and progression of AMD.

Study the effects of reducing zinc in the original AREDS formulation on the development and progression of AMD.

Validate the fundus photographic AMD scale developed from the Age-Related Eye Disease Study.

Enrollment concluded in June 2008 and participants will be followed between five and six years.

If the participant is a current smoker or a former smoker that has quit within the last year, he or she will be randomized to one of the two arms without beta-carotene (Formulations 2 or 3). If a participant does not consent to randomization but wants to take the AREDS formulation, he or she will be provided the supplements provided that they are not a current smoker or a former smoker that has quit within the last year.

Study participants will be assigned randomly to take one of the following Study Supplements on a daily basis: 1) Placebo, 2) Lutein/zeaxanthin, 3) DHA/EPA, or 4) Lutein/zeaxanthin and DHA/EPA.

Primary Randomization Agents

Placebo	Lutein/zeaxanthin	DHA/EPA	Lutein/Zeaxanthin + DHA/EPA
	10 mg/2 mg	350 mg/650 mg	10 mg/2 mg 350 mg/ 650 mg

Participants will be offered the AREDS formulation. Those who agree to take the AREDS formulation and consent to a second randomization will be randomized to receive one of four alternative AREDS formulations in addition to the study supplements described above:

Secondary Randomization Agents (AREDS-Type Supplement)

Formulations	Vitamin C	Vitamin E	Beta Carotene	Zinc Oxide	Cupric Oxide
1	500 mg	400 IU	15 mg	80 mg	2 mg
2	500 m	400 IU	0 mg	80 mg	2 mg
3	500 mg	400 IU	0 mg	25 mg	2 mg
4	500 mg	400 IU	15 mg	25 mg	2 mg

Note: There will be no placebo in this second-tier randomization, as treatment is considered standard of care.

Effects of Long-term Zinc Supplementation on Plasma Thiol Metabolites and Redox Status in Patients With Age-related Macular Degeneration

SIOBHAN E. MORIARTY-CRAIGE, BS, KHOI-NGUYEN HA, BS, PAUL STERNBERG, JR, MD, MICHAEL LYNN, MS, SUSAN BRESSLER, MD, GARY GENSLER, MS, AND DEAN P. JONES, PHD

• PURPOSE: To determine the effects of zinc supplementation on plasma thiol metabolites and their redox status in a cohort of patients with age-related macular degeneration (AMD).
• DESIGN: Randomized clinical trial that evaluated the effects of high doses of zinc and antioxidants on plasma biomarkers of oxidative stress.
• METHODS: This was an ancillary study of the Age-Related Eye Disease Study (AREDS). Subjects with AMD were randomized to one of four treatment groups: (1) antioxidants (vitamin C, 500 mg; vitamin E, 400 IU; and beta carotene, 15 mg), (2) zinc (80 mg zinc oxide, 2 mg cupric oxide), (3) antioxidants plus zinc, or (4) placebo. At 20 and 80 months after randomization, blood specimens were collected and analyzed for glutathione (GSH), oxidized glutathione (GSSG), cysteine (Cys), and cystine (Cy_2SS).
• RESULTS: Although zinc supplementation had no apparent effect on plasma thiol/disulfide redox status at the first blood draw, the group of patients receiving zinc supplementation at the second blood draw had significantly less Cy_2SS compared with those not receiving zinc
• CONCLUSIONS: Because increased Cy_2SS level is associated with aging, oxidative stress, and age-related diseases, the apparent prevention of increased Cy_2SS by zinc supplementation warrants additional investigation.
(Am J Ophthalmol 2007;143:206–211.

ACCUMULATING EVIDENCE IMPLICATES THAT OXIdative stress is involved in the pathogenesis of age-related macular degeneration (AMD); however, no definitive link has yet been established.[1–3] A number of studies have evaluated the potential benefits of antioxidant supplementation in delaying the development and progression of AMD. Results from most observational studies have suggested that intake of antioxidants is associated with a reduction in the risk of AMD development.[4–6] By conducting a randomized, placebo-controlled, two-year clinical trial, Newsome and associates showed that zinc supplementation reduced the risk of vision loss in patients with AMD.[7] This early finding was supported by the Age-Related Eye Disease Study (AREDS),[8] which showed that long-term (6.3 years) intake of zinc, alone or

Known for years

Too much Zinc is bad for us. It actually causes us to age more rapidly.

Most vitamin manufacturers, especially the ones owned and operated by optometrists, reduced their zinc concentrations years ago.

Recent Conclusion

Perceived: AREDS 2 recently concluded that supplementing with Omega 3's did not show any benefit towards halting or reversing macular degeneration.

Actual: The amount of ethyl-ester (Triglyceride form is the natural form) Omega 3 used in the AREDS 2 study did not show any benefits towards halting or reversing macular degeneration.

Eur. J. Lipid Sci. Technol. 2010, *112*, 1315–1322

Research Article

Intestinal digestion of fish oils and ω-3 concentrates under *in vitro* conditions

Diana Martin, Juan A. Nieto-Fuentes, Francisco J. Señoráns, Guillermo Reglero and Cristina Soler-Rivas

Facultad de Ciencias, Sección Departamental de Ciencias de la Alimentación, Universidad Autónoma de Madrid, Cantoblanco, Madrid, Spain

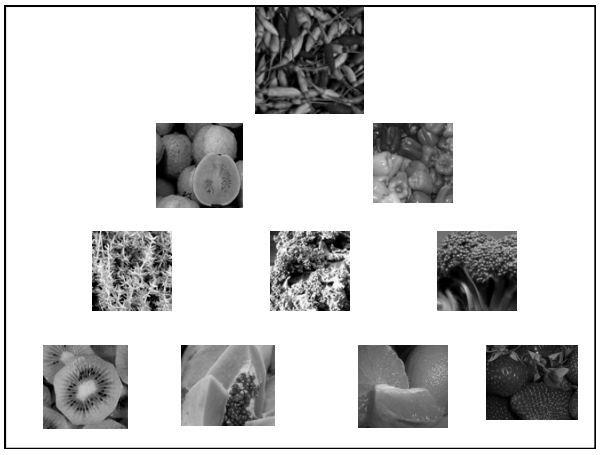
A comparative study of the *in vitro* bioaccesibility of ω-3-oils (salmon oil, SO; tuna oil, TO; enriched-ω-3 oil as triacylglycerols (TAGs), ω-3-TAG; and enriched-ω-3 oil as ethyl esters (EEs), ω-3-EE) was performed after treatment with pancreatin (pancreatic lipase as major lipolytic enzyme) at pH 7.5. Aliquots were taken at different times of digestion for analyzing the evolution of lipid products. The micellar phase (MP) formed at 120 min of digestion was isolated, its total lipid content was extracted and its composition in lipid products was analyzed. The rate of hydrolysis of ω-3-TAG concentrates was continuous throughout the time of reaction (51% hydrolysis of TAGs at 120 min), whereas the digestion of SO and TO was initially faster but stopped after 10 min of reaction (35 and 38% hydrolysis of TAGs at 120 min of SO and TO, respectively). A poor hydrolysis of EEs took place for the ω-3-EE oil (around 7% hydrolysis of EEs at 120 min). The MP of ω-3-TAG oil, SO, and TO mainly consisted of free fatty acids (FFAs) and MAGs. The MP from digested ω-3-EE oil consisted of FFAs and undigested EEs. Therefore, the highest degree of hydrolysis and inclusion of lipid products in the micellar structure was found for the ω-3-TAG oil, but compared to fish oils long times of digestion were required. This experience also shows for the first time the MP composition from ω-3-concentrates in the form of EEs.

AREDS take home message

Antioxidants
Especially Vitamin C
Are beneficial for people
Suffering from ARMD

Top Ten Vitamin C Foods

1. Green Chilis – 245mg/100g
2. Guava – 228mg/100g
3. Bell Peppers – 184mg/100g (341/pepper)
4. Fresh Herbs – Thyme / Parsley – 160mg/100g
5. Green Leafy Vegetables – 120mg/100g
6. Broccoli (Cauliflower / Brussels Sprouts) – 89mg/100g
7. Kiwi – 93 mg/100g
8. Papaya – 62mg/100g
9. Orange – 59mg/100g
10. Strawberry – 59mg/100g



RAW FOODS

Food source in most natural state
Diet rich in fruits and vegetables
Healthy fats via nuts
PH levels naturally increase
Easier to follow due to access

Really???

All participants in AREDS 2 taking a daily multivitamin and/or multimineral supplement will be asked to replace it with Centrum Silver®. This product will be provided free-of-charge (you get what you pay for).

Hippocrates

"If we could give every individual the right amount of nourishment and exercise, not too little and not too much, we would have found the safest way to health."

Contents lists available at SciVerse ScienceDirect

Experimental Gerontology

journal homepage: www.elsevier.com/locate/expgero

Calorie restriction (CR) and CR mimetics for the prevention and treatment of age-related eye disorders ☆

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ARTICLE INFO

Article history:
Received 19 September 2012
Received in revised form 2 February 2013
Accepted 5 April 2013
Available online xxxx

Section Editor: Christiaan Leeuwenburgh

Keywords:
Calorie restriction
Calorie restriction mimetics
Dry eye
Cataract
Retinal disease

ABSTRACT

The morbidity of ocular diseases, including macular degeneration, diabetic retinopathy, and dry eye disease, has been gradually increasing worldwide. Because these diseases develop from age-associated ocular dysfunctions, interventions against the aging process itself may be a promising strategy for their management. Among the several approaches to interrupt aging processes, calorie restriction (CR) has been shown to recover and/or slow age-related functional declines in various organs, including the eye. Here, we review interventions against the aging process as potential therapeutic approaches to age-related ocular diseases. The effects of CR and CR mimetics in animal models of age-related eye diseases are explored. Furthermore, we discuss the possibilities of expanding this research to prospective studies to elucidate the molecular mechanisms by which CR and/or CR mimetics preserve ocular functions.

Ophthalmologica

Original Paper

Ophthalmologica 2005;219:154–166
DOI: 10.1159/000085248

Received: June 17, 2004
Accepted after revision: October 22, 2004

Improvement of Visual Functions and Fundus Alterations in Early Age-Related Macular Degeneration Treated with a Combination of Acetyl-*L*-Carnitine, n-3 Fatty Acids, and Coenzyme Q10

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Phototrop Study

Improvement of Visual Functions and Fundus Alterations in Early Age-Related Macular Degeneration Treated with a Combination of Acetyl- *L -Carnitine, n-3 Fatty Acids, and* Coenzyme Q10

Ophthalmologica 2005;219:154–166)

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Study Medication consisted of 2 oral capsules per day, containing either:

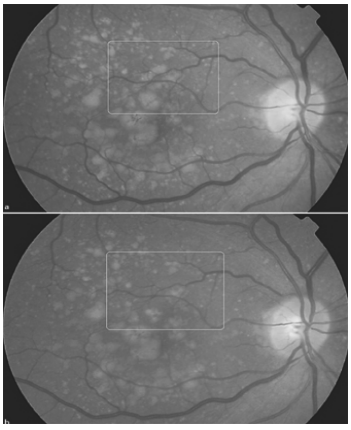
100 mg of ALC
530 mg of n-3FA
10 mg of CoQ10

or
an equal quantity of soy oil.

The aim of this randomized, double-blind, placebo-controlled
clinical trial was to determine the efficacy of a combination of

Acetyl- *L –Carnitine*
n-3 Fatty Acids
and Coenzyme Q10 (Phototrop ®)

on the visual functions and
fundus alterations in early age-related macular degeneration



Inclusion criteria

Have a diagnosis of early bilateral AMD
Have a visual acuity between 8/10 and 4/10
(Snellen chart decimal scale)
Be 55–70 years old and of Caucasian origin
Agree to discontinue any current vitamin regimen
Be highly motivated, alert, oriented, mentally competent and able to understand and comply with the requirements of the study, abide by the restrictions and return for all required visits
Provide written informed consent

Exclusion Criteria

Late AMD (geographic atrophy or macular scarring)
Exudative retinal disease, including exudative AMD
Clinically significant corneal opacity or cataracts
Inherited retinal dystrophies or degenerative myopia
Unstable glaucoma
PVR, rhegmatogenous retinal detachment
Optic nerve disease
Active intraocular inflammatory disease
Refractive error over +4 D and –6 D
Significant cardiovascular or cerebrovascular diseases

Exclusion Criteria

Severe or uncontrolled hepatic, renal, pulmonary, and thyroid disease or diabetes
History of HIV infection, hepatitis B or C, or other immunosuppressive disorders
History of alcoholism, drug abuse, severe mental disorders
Were a practicing vegetarian or had an abnormal diet (<1,600 or >3,500 kcal/day)
Poor general health or unstable diseases
Known or suggested hypersensitivity to study compounds
Use of corticosteroid, phenothiazine and antimalarial drugs within 1 month prior to visit 1 or during the 12-month study period

Acetyl L Carnitine

Acetyl L Carnitine is a supplement to help people burn unwanted or excess body fat. Acetyl L-Carnitine, also known simply as L-Carnitine, transports fatty acids across the inner mitochondra membrane where they are burned and used as energy. Without acetyl L-Carnitine, fatty acids pile up, leading to weight gain. L-Carnitine also helps enhance memory; some people take it to help combat Alzheimer's disease.

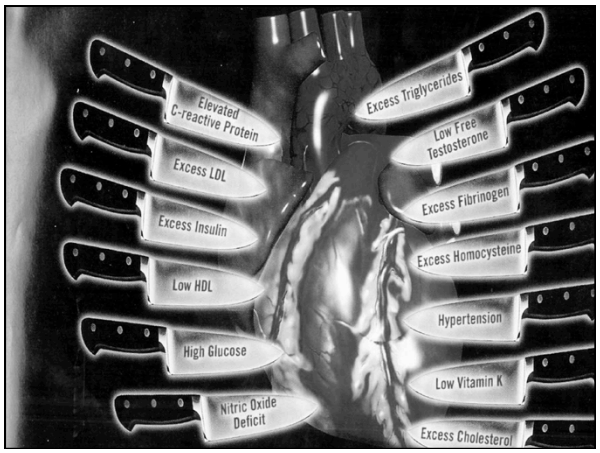
Foods Containing Acetyl L-Carnitine

Organic Grass Fed Beef – 81mg/3oz.
Pork – 24mg/3oz.
Organic Cow's Milk – 8mg/8oz.

Vegetables in general do not make good sources of carnitine. However, there are two vegetables that contain small amounts of carnitine.

Avocados have the largest carnitine count in the vegetable food group, with 2 mg per 1 medium avocado

Six spears of asparagus, or ½ cup, contains .2 mg of carnitine



Co-Q-10

Coenzyme Q10, commonly shortened to CoQ10, is a fat-soluble nutrient found throughout the human body. Recently, CoQ10 has become very popular as a dietary supplement and nutritional medicine. Though evidence is still under investigation, CoQ10 shows promise in preventing or treating common disorders. It is also referred to as ubiquinone

The "Q" in Coenzyme Q-10 refers to quinone, a chemical family that includes CoQ10 and several other biologically essential substances, such as vitamin K1. This is also reflected by the chemical's other name, ubiquinone--a blend of "ubiquitous" because it is found throughout the body, and "quinone" because of its chemical makeup.
CoQ10 is present in nearly every cell of the body, and is collected in cellular mitochondria. It is an essential part of the process of cellular respiration, which creates ATP, the nucleotide responsible for nearly all of the body's energy production. Though it is found throughout the body, CoQ10 is most highly concentrated in the organs that require the most energy transfer,

such as the heart

Cholesterol lowering agents

Deplete our body of

Vitamin A
Vitamin B12
Vitamin D
Vitamin E
Vitamin K

Co-Q-10

Beta-Carotene
Folic acid
Iron

Implications of statin adverse effects in the elderly

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The elderly differ from younger people in the relation of cholesterol to heart disease and mortality. Clinical trial evidence supports epidemiological findings in showing that high cholesterol weakens in its relationship to heart disease with age and loses (and in older age reverses) its relation to mortality. Randomised trial data confirm that lowering cholesterol no longer extends life in the elderly, even those at high risk of heart disease, and no evidence supports the presumption that the impact on all-cause morbidity is any more favourable. These findings increase the importance of statin adverse effects (AEs) in this group. Furthermore, the elderly may be more vulnerable to known AEs, and evidence provides cause for concern that new risks may supervene, including cancer, neurodegenerative disease and heart failure. Physiological evidence regarding the impact of statins on mitochondrial function, and mitochondrial function on ageing, support these concerns. Additionally, the impact of statin AEs (e.g., muscle and cognitive problems) may be amplified in this group. Effects may be misattributed to ageing. Even modestly lower cognitive and physical function in older elderly prognosticates increased disability, hospitalisation, institutionalisation, and mortality. Disability, once present, is less likely to recover. Because the risk for AEs is unattended by evidence of net benefit to the person, the use of statins in the elderly should be undertaken, if at all, with circumspection and close scrutiny for adverse effects.

Table 3
Comparison of adverse effects and food/drug interactions between red yeast rice and statins

Drug	Metabolic effect	Adverse effects	Food interaction	Drug interaction
Red yeast rice	↓TC, TG, LDL ↑ HDL	Allergy, heart burn, abdominal discomfort, flatulence, and dizziness	None reported. In theory, same as lovastatin	None reported. In theory, same as lovastatin
Statins:				
Atorvastatin (Lipitor™)	↓TC, TG, LDL, and VLDL ↑ HDL; ↑ liver E, ↓CoE Q_{10}	Nausea, dyspepsia, abdominal and muscle pain, constipation, flatulence, rash, oedema, dizziness, chest pain, insomnia	Grapefruit juice, Alcohol	With ↑ dose of niacin, myopathy
Fluvastatin (Lescol™)	↓TC, TG, LDL, ↑ HDL, ↑ liver E	Dyspepsia, nausea, abdominal cramps, headache, insomnia, muscle pain	None reported	With ↑ dose of niacin, myopathy
Lovastatin (Mevacor™)	↓TC, TG, LDL, and VLDL ↑ HDL, ↑ liver E, ↑ CPK, ↓CoE Q_{10}	Nausea, dyspepsia, abdominal pain, constipation, flatulence, headache, rash, blurred vision, dizziness, muscle pain, insomnia, rare rhabdomyolysis	Grapefruit juice, alcohol, fibre, pectin, and oat bran	With ↑ dose of niacin, myopathy
Pravastatin (Pravachol™)	↓TC, TG, LDL, and VLDL ↑ HDL, ↓CoE Q_{10}	Nausea, vomiting, diarrhoea, headache, muscle pain, rash	Alcohol	With ↑ dose of niacin, myopathy
Simvastatin (Zocor™)	↓TC, TG, LDL, and VLDL, ↑ HDL, ↓CoE Q_{10}	Dyspepsia, constipation, muscle pain, insomnia, rare rhabdomyolysis	Grapefruit juice, alcohol	With ↑ dose of niacin, myopathy

( ): brand names; TC: total cholesterol; TG: triglycerides; HDL: high-density lipoprotein; LDL: low-density lipoprotein; VLDL: very low-density lipoprotein; liver E: liver enzymes (SGOT, SGTP); CoE Q_{10}: coenzyme Q_{10}; CPK: creatine phosphokinase.

Foods That Contain Co-Q-10

Organic, grass fed meats contain a high concentration of CoQ10. A report from Iowa State University lists beef, chicken and pork as all containing between 1.2 and 2.6 milligrams (mg) of CoQ10 in a three ounce serving, with beef containing the most at 2.6 mg per serving. Fish also contain higher levels of CoQ10. Marinated herring is listed by the Linus Pauling Institute (LPI) as containing 2.3 mg per three ounce serving. Following herring is rainbow trout at 0.9 mg and salmon at 0.4 mg per three ounce serving.

Phototrope Study Results

Improvement was found in each of the four parameters of *visual functions in the most affected eyes of EARLY AMD* patients taking Phototrop. It is particularly important that VFMD (Visual Field Mean Deviation, the primary efficacy variable), visual acuity and foveolar sensitivity (secondary efficacy variables) showed statistically significant differences in changes comparing treated with placebo groups.

Table 4. Distribution of changes in the drusen-covered area

	Most affected eyes		Less affected eyes	
	treated (n = 46)	placebo (n = 52)	treated (n = 4)	placebo (n = 44)
Improved or unchanged	38 (83%)	39 (75%)	42 (91%)	31 (70%)
Deteriorated	8 (17%)	13 (25%)	4 (9%)	13 (30%)
p	0.25		0.01	
Odds ratio	1.58		4.40	

Table 2. Comparison of changes in visual field mean defect of the most and less affected eyes[a]

	Most affected eyes		Less affected eyes[b]	
	treated (n = 48)	placebo (n = 53)	treated (n = 43)	placebo (n = 45)
Improved or unchanged	47 (98%)	44 (83%)	43 (100%)	40 (89%)
Deteriorated	1 (2%)	9 (17%)	0 (0%)	5 (11%)
p	0.006		0.031	
Odds ratio	10.93		11.81	

[a] ± 2.0 dB long-term fluctuation was applied.
[b] Data were modified by adding 0.5 to each value in the less affected eyes for odds ratio computing.

Fig. 3. Comparison of changes in the drusen-covered area (ratio of 12-month values to baseline) showed statistically significant differences between 'treated' and 'placebo' groups of both the most affected eyes and the less affected eyes (0.85 ± 0.39 vs. 1.11 ± 0.65, p = 0.045 and 0.77 ± 0.43 vs. 1.13 ± 0.77, p = 0.017, respectively).

ELSEVIER

CURRENT RESEARCH

EDWARD COTLIER AND ROBERT WEINREB, EDITORS

Transport and Retinal Capture of Lutein and Zeaxanthin with Reference to Age-related Macular Degeneration

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Abstract. Age-related macular degeneration (AMD) is the most common cause of irreversible blindness in the elderly population in the western world. The etiology and pathogenesis of this disease remain unclear. However, there is an increasing body of evidence supporting the hypothesis that the macular pigment carotenoids, lutein and zeaxanthin, play an important role in protection against AMD, by filtering out blue light at a pre-receptoral level, or by quenching free radicals. Lutein and zeaxanthin are dietary xanthophyll carotenoids, which are delivered to the retina via plasma lipoproteins. The biological mechanisms governing retinal capture and accumulation of lutein and zeaxanthin, to the exclusion of other carotenoids, are still poorly understood. Although these mechanisms remain unclear, it is possible that selective capture of these carotenoids is related to lipoprotein, or apolipoprotein, function and profile. Xanthophyll-binding proteins appear to play an important role in the retinal capture of the xanthophyll carotenoids. The Pi isoform of GSTP1 has been isolated as a specific binding protein for zeaxanthin. The binding protein responsible for retinal uptake of lutein remains elusive. This article reviews the literature germane to the mechanisms involved in the capture, accumulation and stabilization of lutein and zeaxanthin by the retina, and the processes involved in their transport in serum. (**Surv Ophthalmol 53**:68–81, 2008.

Transport and Retinal Capture of Lutein and Zeaxanthin with Reference to ARMD

Survey of Ophthalmology
Volume 53 No. 1 Jan-Feb 2008

Absorption

Several processes are required for optimal absorption of carotenoids. These include adequate digestion of the food matrix in order to release the carotenoids, formation of lipid micelles in the small intestine, uptake of the carotenoid by intestinal mucosal cells, and transport of carotenoids to the lymphatic or portal circulation.

Transport

The majority of plasma carotenoids are transported on LDL, with 55% of total carotenoids associated with it, whereas HDL is associated with 33% and VLDL 10-19% respectively

Lutein and Zeaxanthin are equally distributed between LDL + HDL molecules

Capture

Retinal capture of the xanthophyll carotenoids is mediated largely by a specific xanthophyll binding protein (XBP), specifically the Pi isoform of GSTP1 in the case of zeaxanthin. The specific binding protein for lutein remains elusive.

Conclusion

The authors concluded that in order to fully explore the potential beneficial effects of lutein and zeaxanthin, in particular in the context of their punitive role in the prevention of AMD, it is essential that we understand the mechanisms by which they are absorbed from the GI system, transported in the serum and taken up by the retina.

Double-masked, placebo-controlled, randomized trial of lutein and antioxidant supplementation in the intervention of atrophic age-related macular degeneration: the Veterans LAST study (Lutein Antioxidant Supplementation Trial)

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Background: Age-related macular degeneration (ARMD) is the leading cause of vision loss in aging Western societies. The objective of the lutein antioxidant supplementation trial (LAST) is to determine whether nutritional supplementation with lutein or lutein together with antioxidants, vitamins, and minerals improves visual function and symptoms in atrophic ARMD.

Methods: The study was a prospective, 12-month, randomized, double-masked, placebo-controlled trial conducted at an urban midwestern Veterans Administration Hospital from August 1999 to May 2001. Ninety patients with atrophic ARMD were referred by ophthalmologists at two Chicago-area veterans medical facilities. Patients in Group 1 received lutein 10 mg (L); in Group 2, a lutein 10 mg/antioxidants/vitamins and minerals broad spectrum supplementation formula (L/A); and in Group 3, a maltodextrin placebo (P) over 12 months.

Results: In Groups 1 L and 2 L/A, mean eye macular pigment optical density increased approximately 0.09 log units from baseline, Snellen equivalent visual acuity improved 5.4 letters for Group 1 L and 3.9 letters for Group 2 L/A, and contrast sensitivity improved. There was a net subjective improvement in Amsler grid in Group 1 L. VFQ-14 questionnaires concerning subjective glare recovery were nearly significant at 4 months for Group 2 L/A. Patients who received the placebo (Group 3) had no significant changes in any of the measured findings.

Conclusion: In this study, visual function is improved with lutein alone or lutein together with other nutrients. Further studies are needed with more patients, of both genders, and for longer periods of time to assess long-term effects of lutein or lutein together with a broad spectrum of antioxidants, vitamins, and minerals in the treatment of atrophic age-related macular degeneration.

Age-related macular degeneration (ARMD) is the leading cause of untreated vision loss in aging Western societies, accounting for 45% of all visual disability in the United States.[1] Increasing age is associated with increasing prevalence of ARMD.[2] Atrophic ARMD constitutes 90% of all cases. It results in a chronic, painless, bilateral asymmetric, paracentral, or central photoreceptor-retinal pigment epithelium (RPE) disturbance.[3] ARMD has increased in prevalence in Great Britain in the last 60 years, suggesting that genetic predisposition is not the primary etiologic factor.[4] In Japan, the prevalence of ARMD is increasing, possibly from a shift to a more-Westernized diet.[5]

ARMD is a complex disorder that involves genetic, cardiovascular, environmental, and nutritional components. Recent identification of a locus on chromosome 1q31 associated with increased susceptibility to ARMD may some day allow testing of high-risk individuals.[6] After aging, smoking remains the most significant risk factor for ARMD.[7,8] Smoking is known to deplete serum antioxidants, alter blood viscosity, alter the auto regulation flow mechanism of blood vessels, and is associated with lower levels of macular xanthophylls pigments, such as lutein.[9,10] Environmental risk factors include exposure to solar radiation/blue light and photosensitizing drugs.[11-14]

LAST study

Double-masked, placebo-controlled, randomized trial of lutein and antioxidant supplementation in the intervention of atrophic ARMD: the Veterans LAST study

(**L**utein **A**ntioxidant **S**upplementation **T**rial)

Optometry Vol. 75 No. 4

Table 1. Baseline characteristics

Variable	Lutein (n = 29)	Lutein/A (n = 30)	Placebo (n = 31)	P value
Sex Male	27	29	30	—
Female	2	1	1	—
Age, mean (SD), yrs.	74.4 (6.4)	73.5 (8.5)	76.1 (6.4)	0.34
ARMD Dx mean (SD), yrs.	4.1 (5.2)	4.4 (4.4)	4.9 (5.9)	0.82
Smoking pack-years	5.2 (14.1)	7.1 (17.3)	9.2 (22.6)	0.71
Alcohol grams	11.0 (26.7)	11.9 (17.8)	6.3 (11.8)	0.52
Caffeine mg	231 (192)	225 (247)	211 (171)	0.32
Body Mass Index	28.5 (4.2)	30.4 (4.8)	27.3 (5.7)	0.06
Iris color				
Blue/Gray – light (n)	13	14	18	0.63
Gray/Hazel – light (n)	9	6	3	0.22
Brown/Black – dark (n)	7	10	9	0.76
Multivitamin use				
None (n)	14	13	14	0.97
Pabuum (n)	7	8	9	0.88
RDA+ (n)	8	9	8	0.96
Dietary Zn include	18.5 (16)	16.3 (13)	30.7 (33)	0.04
Supplements mg				
Dietary lutein mg	3.0 (2.6)	2.1 (1.4)	1.9 (1.6)	0.13
Dietary iron mg *	17.7 (18)	22.2 (34)	23.7 (19)	0.70
Ocular Baseline Data and Significance				
Cataract (R LOCSIII rating)				
Nuclear color	28.3 (1.03)	3.26 (1.13)	2.86 (1.09)	0.28
Nuclear opalescence	2.73 (0.96)	3.30 (1.14)	2.78 (1.12)	0.11
Cortical	1.83 (1.07)	1.56 (0.80)	1.56 (0.82)	0.48
Posterior subcapsular	1.04 (0.21)	1.04 (0.19)	1.00 (0.00)	0.56
Cataract (L LOCSIII rating)				
Nuclear color	2.81 (0.85)	3.15 (0.99)	3.00 (1.31)	0.51
Nuclear opalescence	2.73 (0.87)	3.15 (0.99)	2.92 (1.36)	0.39
Cortical	1.73 (0.87)	1.41 (0.70)	1.75 (1.01)	0.27
Posterior subcapsular	1.12 (0.43)	1.04 (0.19)	1.21 (0.78)	0.47

AREDS, mean retinal photographic grade and distribution (percent)

R AREDS retinal grade, mean		3.33 (0.62)	2.88 (1.03)	3.06 (0.90)	0.51
R Eyes	% Grade I	4.5	11.1	0.0	0.002
	% Grade II	18.2	16.7	12.0	0.51
	% Grade III	46.4	44.4	56.0	0.43
	% Grade IV	31.8	27.8	32.0	0.83
L Eyes retinal grade, mean		2.85 (0.55)	2.71 (1.2)	3.28 (0.83)	0.13
L Eyes	% Grade I	0.0	4.5	4.2	0.10
	% Grade II	36.4	31.8	16.7	0.02
	% Grade III	54.5	40.1	37.5	0.15
	% Grade IV	9.1	22.7	41.7	0.0002
MPOD †	R	0.23 (0.14)	0.16 (0.08)	0.23 (0.14)	0.05
	L	0.24 (0.16)	0.21 (0.12)	0.24 (0.15)	0.63
Visual Baseline Data and Significance					
Visual acuity	R (LogMar)	0.359	0.324	0.445	0.19
	L (LogMar)	0.279	0.303	0.286	0.15
Glare recovery R (sec)		100.7 (65.1)	88.7 (58.2)	73.4 (54.4)	0.34
recovery L (sec)		83.4 (59.2)	82.2 (64.0)	89.7 (65.2)	0.92
Contrast sensitivity R					
3 cc/degree (log)		1.55 (0.28)	1.53 (0.23)	1.62 (0.30)	0.52
6 cc/degree (log)		1.56 (0.35)	1.46 (0.33)	1.65 (0.28)	0.14
12 cc/degree (log)		1.10 (0.34)	1.06 (0.43)	1.20 (0.42)	0.47
18 cc/degree (log)		0.60 (0.38)	0.55 (0.34)	0.64 (0.44)	0.70
Contrast sensitivity L					
3 cc/degree (log)		1.63 (0.24)	1.51 (0.20)	1.62 (0.21)	0.10
6 cc/degree (log)		1.55 (0.21)	1.51 (0.32)	1.56 (0.25)	0.80
12 cc/degree (log)		1.07 (0.36)	1.08 (0.36)	1.10 (0.36)	0.97
18 cc/degree (log)		0.54 (0.42)	0.50 (0.29)	0.51 (0.32)	0.95
Amsler grid defects R (n)		15	10	11	0.56
	L (n)	11	18	11	0.29

SD, Standard deviation; ***ARMD Dx***, years diagnosed with atrophic age-related macular degeneration; ***RDA+***, vitamin consumption beyond the Recommended Daily Allowance; ***LOCSIII***, Lens Opacity Classification System, 3rd revision; ***AREDS***, NIH National Eye Institute Age-Related Eye Disease Study; ***MPOD***, macular pigment optical density; and ***LogMar***, log minimal angle of resolution.
Smoking status included present and past smoking, and not exposure to passive (second-hand) smoke. Eye color was assessed by categorical visual inspection (blue/gray, gray/hazel, and brown/black) under identical lighting conditions.
* Serum iron, transferrin saturation, ferritin, and total iron binding capacity (n = 75) published separately.[9] Additional postulated independent ARMD (and cardiovascular) risk factors obtained (n = 25) by SSDI, Laboratories, Asheville, North Carolina. Fibrinogen was elevated at 409 ± 89%; homocysteine was elevated at 13.6 ± 9.2 mg %; and C-reactive protein was slightly elevated at 2.3 ± 4.9 mg % against SSDI normative data.
† *R* (right eye) and *L* (left eye) baseline MPOD are correlated, describing 49% of the variance of macular pigmentation in this veteran population. Low spatial frequency contrast sensitivity (3 cc/degree – large object vision) is weakly positively correlated with MPOD (Pearson $r = 0.28$; $P = 0.02$).[48]

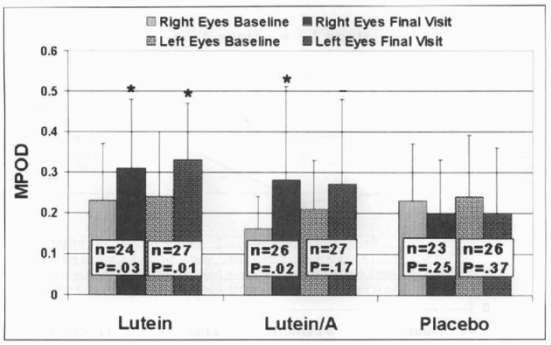


Figure 1 Primary Outcome Intervention Data: mean (SD) macular pigment ocular density (MPOD) by intervention group at baseline and final study visit. Mean eye MPOD improved 36% in the lutein group, 43% in the lutein/antioxidant group, and mildly decreased in the placebo group. Paired *t* test *P* values shown: *n* = number of eyes.

Conclusion

The LAST study concluded that visual function is improved with lutein alone or lutein together with other nutrients.

Foods That Contain Lutein

Vegetable/Fruit	Lutein or Zeaxanthin (Micrograms) (100 grams or 1/2 cup)
Kale	21900
Collard Greens	16,300
Spinach, cooked & drained	12,600
Cress Leaf raw	12,500
Swiss Chard raw	11,000
Chicory Leaf raw	10,300
Parsley	10,200
Spinach raw	10,200

Foods That Contain Lutein

Vegetable/Fruit	Lutein or Zeaxanthin (Micrograms) (100 grams or 1/2 cup)
Mustard Greens	9,900
Beet Greens	7,700
Okra	6,800
Red Pepper	6,800
Dill	6,700
Romaine Lettuce	5,700
Endive	4,000
Celery	3,600
Scallions	2,100
Leeks	1,900
Broccoli, cooked	1,800

LAST 2 study

Differential temporal responses of macular pigment optical density in patients with atrophic ARMD to dietary supplementation with xanthophylls

Optometry (2007) 78, 213-219

Stuart Richer, O.D., Ph.D. Jenny Devenport, Ph.D. John C. Lang. Ph.D.

LAST 2 study Objective

The LAST study was to determine whether specific dietary interventions increased macular pigment optical density (MOPD) and visual function in patients with atrophic ARMD.

The LAST 2 objective is to discern those specific characteristics that increase MPOD.

LAST 2 Results

MPOD increased with supplementation and decreased without. The highest increases in MOPD over time occurred in patients with lower baseline values of MPOD.

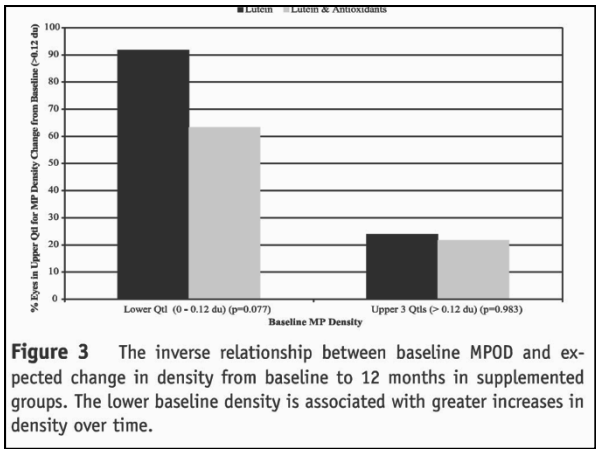
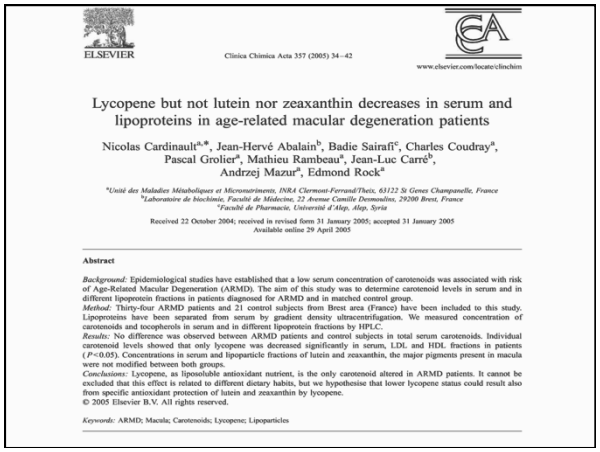


Figure 3 The inverse relationship between baseline MPOD and expected change in density from baseline to 12 months in supplemented groups. The lower baseline density is associated with greater increases in density over time.

LAST 2 Conclusion

Noteworthy is the observation that those individuals with the lowest MPOD, and in greatest need of supplementation, were also most likely to benefit from either lutein or lutein plus antioxidant supplementation.



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Clinica Chimica Acta 357 (2005) 34–42

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Lycopene but not lutein nor zeaxanthin decreases in serum and lipoproteins in age-related macular degeneration patients

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Received 22 October 2004; received in revised form 31 January 2005; accepted 31 January 2005
Available online 29 April 2005

Abstract

Background: Epidemiological studies have established that a low serum concentration of carotenoids was associated with risk of Age-Related Macular Degeneration (ARMD). The aim of this study was to determine carotenoid levels in serum and in different lipoprotein fractions in patients diagnosed for ARMD and in matched control group.
Method: Thirty-four ARMD patients and 21 control subjects from Brest area (France) have been included to this study. Lipoproteins have been separated from serum by gradient density ultracentrifugation. We measured concentration of carotenoids and tocopherols in serum and in different lipoprotein fractions by HPLC.
Results: No difference was observed between ARMD patients and control subjects in total serum carotenoids. Individual carotenoid levels showed that only lycopene was decreased significantly in serum, LDL and HDL fractions in patients ($P<0.05$). Concentrations in serum and lipoparticle fractions of lutein and zeaxanthin, the major pigments present in macula were not modified between both groups.
Conclusions: Lycopene, as liposoluble antioxidant nutrient, is the only carotenoid altered in ARMD patients. It cannot be excluded that this effect is related to different dietary habits, but we hypothesise that lower lycopene status could result also from specific antioxidant protection of lutein and zeaxanthin by lycopene.

Keywords: ARMD; Macula; Carotenoids; Lycopene; Lipoparticles

Lycopene but not Lutein nor Zeaxanthin decreases in serum lipoproteins in ARMD patients

Clinica Chimica Acta 357 (2005) 34-42

Study Objectives

Epidemiological studies have established that a low serum concentration of carotenoids was associated with ARMD. The aim of this study was to determine carotenoid levels in serum and in different lipoprotein fractions in patients diagnosed with ARMD and in a matched control group.

Results

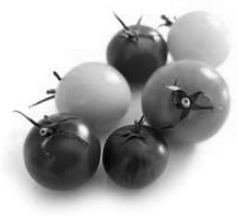
No difference was observed between ARMD patients and the control subjects in total serum carotenoids.

Concentrations in serum and lipoparticle fractions of lutein + Zeaxanthin were also equal between the two groups.

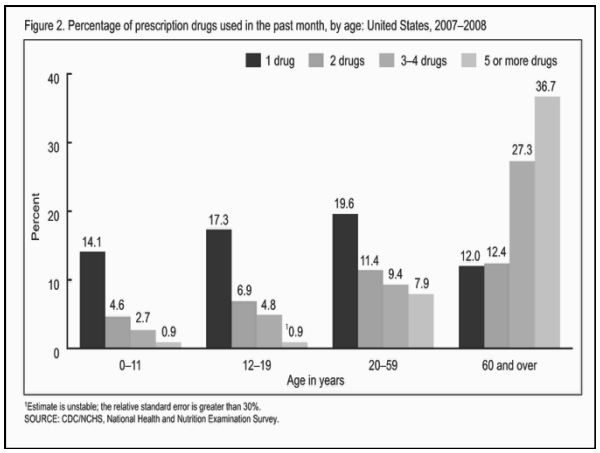
Serum and lipoparticle fractions of Lycopene was significantly decreased in ARMD patients.

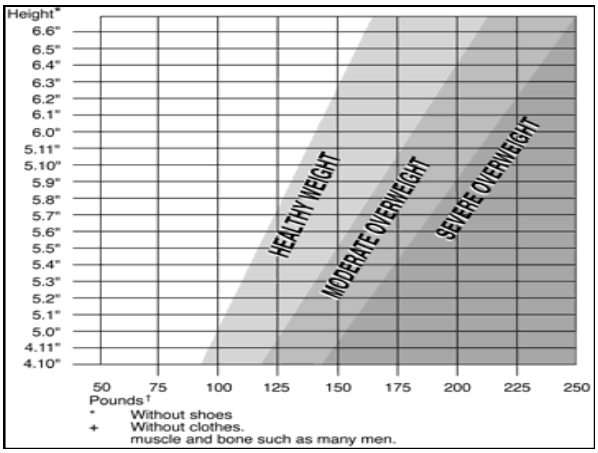
Conclusion

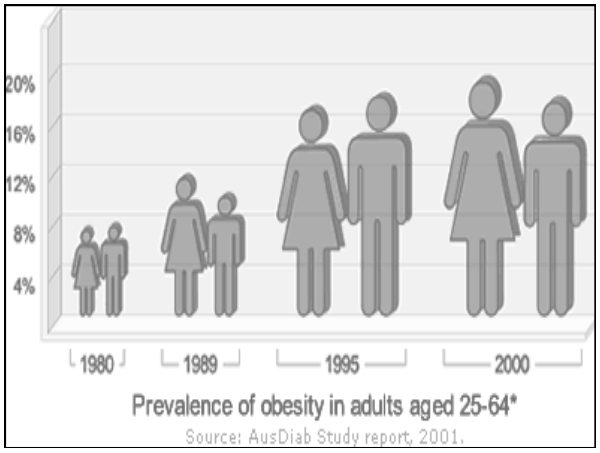
Lycopene, a liposoluble antioxidant nutrient, is the only carotenoid altered in ARMD patients.



There he goes talking about fresh fruits again







Trends of Enormous Proportions

BMI	1986	2000
BMI 30 - 35	1 in 10	1 in 5
BMI at least 40	1 in 200	1 in 50
BMI 50+	1 in 2000	1 in 400

Source: Archives of Internal Medicine, October, 2003

Plato

"We shall eat animals only at our own peril."

Risk Reduction Recommendations

Reduce
Weight
Stress
Smoking
Rx medications

Increase
Exercise
Awareness of Diet
Level of Happiness
Supplement Use

Cigarette Smoking and the Natural History of Age-Related Macular Degeneration

The Beaver Dam Eye Study

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Purpose: To examine the association of current cigarette smoking and pack-years smoked with the incidence and progression of age-related macular degeneration (AMD) and to examine the interactions of current smoking and pack-years smoked with *complement factor H* (*CFH*, rs1061170) and *age-related maculopathy susceptibility 2* (*ARMS2*, rs10490924) genotype.
Design: A longitudinal population-based study of AMD in a representative American community. Examinations were performed every 5 years over a 20-year period.
Participants: A total of 4439 participants in the population-based Beaver Dam Eye Study (BDES).
Methods: Age-related macular degeneration status was determined from grading retinal photographs. Multistate models were used to model the relationship of current smoking and pack-years smoked and interactions with *CFH* and *ARMS2* with the incidence and progression of AMD over the entire age range.
Main Outcome Measures: Incidence and progression of AMD over a 20-year period and interactions between current smoking and pack-years smoked with *CFH* and *ARMS2* genotype.
Results: The incidence of early AMD over the 20-year period was 24.4%, and the incidence of late AMD was 4.5%. Current smoking was associated with an increased risk of transitioning from minimal to moderate early AMD. A greater number of pack-years smoked was associated with an increased risk of transitioning from no AMD to minimal early AMD and from severe early AMD to late AMD. Current smoking and a greater number of pack-years smoked were associated with an increased risk of death. There were no statistically significant multiplicative interactions between current smoking or pack-years smoked and *CFH* or *ARMS2* genotype.
Conclusions: Current smoking and a greater number of pack-years smoked increase the risk of the progression of AMD. This has important health care implications because smoking is a modifiable behavior. *Ophthalmology 2014;121:1949-1955 © 2014 by the American Academy of Ophthalmology.*

Vision Research

journal homepage: www.elsevier.com/locate/visres

Cigarette smoking, oxidative stress, the anti-oxidant response through Nrf2 signaling, and Age-related Macular Degeneration

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ARTICLE INFO

Article history:
Received 25 June 2009
Received in revised form 7 August 2009

Keywords:
Age-related Macular Degeneration

ABSTRACT

Age-related Macular Degeneration (AMD) is the leading cause of blindness among the elderly. While excellent treatment has emerged for neovascular disease, treatment for early AMD is lacking due to an incomplete understanding of the early molecular events. Cigarette smoking is the strongest epidemiologic risk factor, yet we do not understand how smoking contributes to AMD. Smoking related oxidative damage during the early phases of AMD may play an important role. This review explores how cigarette smoking and oxidative stress to the retinal pigmented epithelium (RPE) might contribute to AMD, and

Journal of Cardiac Failure Vol. 16 No. 9 2010

Yoga in Heart Failure Patients: A Pilot Study

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ABSTRACT

Background: Complementary therapies such as yoga practice have become commonplace, yet the safety, physical, and psychological effects on patients with heart failure (HF) are unknown. The purpose of this study was to determine whether an 8-week yoga program was safe and would positively influence physical and psychological function in HF patients.

Methods and Results: Stable HF patients were recruited (n = 15) and completed (n = 12) 8 weeks of yoga classes. Data collected were: safety (cardiac and orthopedic adverse events); physical function (strength, balance, endurance, flexibility); and psychological function (quality of life [QOL], depression scores, mindfulness) before and after 8 weeks of yoga classes.

Results: Mean age was 52.4 ± 11.6 with three-fourths (n = 9) being male and Caucasian. No participant had any adverse events. Endurance ($P < .02$) and strength (upper $P = .04$ and lower body $P = .01$) significantly improved. Balance improved by 13.6 seconds (26.9 ± 19.7 to 40.0 ± 18.5; $P = .05$). Symptom stability, a subscale of QOL, improved significantly ($P = .02$). Although no subject was depressed, overall mood was improved. Subjects subjectively reported improvements in overall well-being.

Conclusions: Yoga practice was safe, with participants experiencing improved physical function and symptom stability. Larger studies are warranted to provide more nonpharmacological options for improved outcomes in patients with HF. (*J Cardiac Fail 2010;16:742–749*)

Key Words: Physical function, quality of life, balance, endurance.

Randomized Controlled Clinical Trial of Yoga in the Treatment of Eating Disorders

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Manuscript received March 27, 2009; manuscript accepted August 25, 2009

Abstract

Purpose: This was a pilot project designed to assess the effect of individualized yoga treatment on eating disorder outcomes among adolescents receiving outpatient care for diagnosed eating disorders (anorexia nervosa, bulimia nervosa, eating disorder not otherwise specified).

Methods: A total of 50 girls and 4 boys aged 11–21 years were randomized to an 8-week trial of standard care vs. individualized yoga plus standard care. Of these, 27 were randomized to standard care and 26 to yoga plus standard care (attrition: n = 4). Standard care (every other week physician and/or dietician appointments) was required to meet ethical guidelines. The No Yoga group was offered yoga after study completion as an incentive to maintain participation. Outcomes evaluated at baseline, end of trial, and 1-month follow-up included Eating Disorder Examination (EDE), Body Mass Index (BMI), Beck Depression Inventory, State-Trait Anxiety Inventory, and Food Preoccupation questionnaire.

Results: The Yoga group demonstrated greater decreases in eating disorder symptoms. Specifically, the EDE scores decreased over time in the Yoga group, whereas the No Yoga group showed some initial decline but then returned to baseline EDE levels at week 12. Food preoccupation was measured before and after each yoga session, and decreased significantly after all sessions. Both groups maintained current BMI levels and decreased in anxiety and depression over time.

Conclusions: Individualized yoga treatment decreased EDE scores at 12 weeks, and significantly reduced food preoccupation immediately after yoga sessions. Yoga treatment did not have a negative effect on BMI. Results suggest that individualized yoga therapy holds promise as adjunctive therapy to standard care.

Physiology & Behavior xxx (2012) xxx–xxx

Contents lists available at SciVerse ScienceDirect

Physiology & Behavior

journal homepage: www.elsevier.com/locate/phb

Adiponectin, leptin, and yoga practice☆

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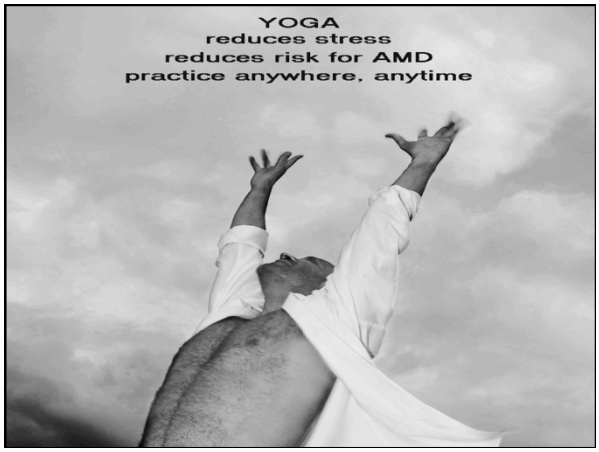
ARTICLE INFO

Article history:
Received 13 October 2011
Received in revised form 14 January 2012
Accepted 20 January 2012
Available online xxxx

Keywords:
Adiponectin
Leptin
yoga
Inflammation
Psychoneuroimmunology
Complementary medicine

ABSTRACT

To address the mechanisms underlying hatha yoga's potential stress-reduction benefits, we compared adiponectin and leptin data from well-matched novice and expert yoga practitioners. These adipocytokines have counter-regulatory functions in inflammation; leptin plays a proinflammatory role, while adiponectin has anti-inflammatory properties. Fifty healthy women (mean age = 41.32, range = 30–65), 25 novices and 25 experts, provided fasting blood samples during three separate visits. Leptin was 36% higher among novices compared to experts, $P = .008$. Analysis of adiponectin revealed a borderline effect of yoga expertise, $P = .08$; experts' average adiponectin levels were 28% higher than novices across the three visits. In contrast, experts' average adiponectin to leptin ratio was nearly twice that of novices, $P = .009$. Frequency of self-reported yoga practice showed significant negative relationships with leptin; more weeks of yoga practice over the last year, more lifetime yoga sessions, and more years of yoga practice were all significantly associated with lower leptin, with similar findings for the adiponectin to leptin ratio. Novices and experts did not show even marginal differences on behavioral and physiological dimensions that might represent potential confounds, including BMI, central adiposity, cardiorespiratory fitness, and diet. Prospective studies addressing increased risk for type II diabetes, hypertension, and cardiovascular disease have highlighted the importance of these adipocytokines in modulating inflammation. Although these health risks are clearly related to more extreme values then we found in our healthy sample, our data raise the possibility that longer-term and/or more intensive yoga practice could have beneficial health consequences by altering leptin and adiponectin production.



SURVEY OF OPHTHALMOLOGY VOLUME 54 • NUMBER 3 • MAY–JUNE 2009

MAJOR REVIEW

Effects of Exercise on Ocular Physiology and Disease

Jesse Gale, MB ChB,[1] Anthony P. Wells, FRANZCO,[1,2] and Graham Wilson, FRANZCO[3]

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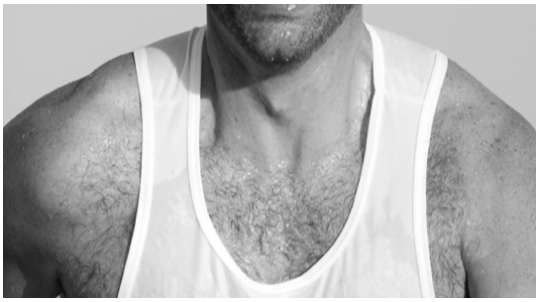
Abstract. Regular exercise is a healthy lifestyle choice with numerous benefits to general health. Ophthalmologists may face questions of the benefits or risks of exercise to eyes. Here the effects of acute exertion and regular physical activity on ocular physiology and disease are reviewed. Intraocular pressure is transiently reduced by dynamic exercise. For the great majority of patients exercise is beneficial to the eyes by reducing risk of central retinal vein occlusion and neovascular age-related macular degeneration, and by improving control of systemic hypertension and diabetes. Ophthalmologists should be advocates of regular exercise with appropriate eye protection. (**Surv Ophthalmol 54**:349–355, 2009.



Published in final edited form as:
Curr Hypertens Rep. 2007 December ; 9(6): 520–528.

Stress Reduction Programs in Patients with Elevated Blood Pressure: A Systematic Review and Meta-analysis

Maxwell V. Rainforth, PhD, Robert H. Schneider, MD, Sanford I. Nidich, EdD, Carolyn Gaylord-King, PhD, John W. Salerno, PhD, and James W. Anderson, MD

Abstract

Substantial evidence indicates that psychosocial stress contributes to hypertension and cardiovascular disease (CVD). Previous meta-analyses of stress reduction and high blood pressure (BP) were outdated and/or methodologically limited. Therefore, we conducted an updated systematic review of the published literature and identified 107 studies on stress reduction and BP. Seventeen trials with 23 treatment comparisons and 960 participants with elevated BP met criteria for well-designed randomized controlled trials and were replicated within intervention categories. Meta-analysis was used to calculate BP changes for biofeedback, −0.8/−2.0 mm Hg (P = NS); relaxation-assisted biofeedback, +4.3/+2.4 mm Hg (P = NS); progressive muscle relaxation, −1.9/−1.4 mm Hg (P = NS); stress management training, −2.3/−1.3 mm (P = NS); and the Transcendental Meditation program, −5.0/−2.8 mm Hg (P = 0.002/0.02). Available evidence indicates that among stress reduction approaches, the Transcendental Meditation program is associated with significant reductions in BP. Related data suggest improvements in other CVD risk factors and clinical outcomes.

Published in final edited form as:
Cardiol Rev. 2004 ; 12(5): 262–266.

Review of Controlled Research on the Transcendental Meditation Program and Cardiovascular Disease:

Risk Factors, Morbidity, and Mortality

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Abstract

Because of growing evidence for stress as a major factor contributing to cardiovascular disease (CVD), techniques of meditation are being increasingly used. The Transcendental Meditation (TM) technique is distinct from other techniques of meditation not only in its origin and procedure, but also in the amount and breadth of research testing it. Evidence for its ability to reduce traditional and novel risk factors for CVD includes: 1) decreases in blood pressure, 2) reduced use of tobacco and alcohol, 3) lowering of high cholesterol and lipid oxidation, and 4) decreased psychosocial stress. Changes expected to result from reducing these risk factors, namely, reversal of atherosclerosis, reduction of myocardial ischemia and left ventricular hypertrophy, reduced health insurance claims for CVD, and reduced mortality, also have been found with TM practice. Research on mechanisms suggests that some of the CVD-related benefits as a result of this technique could arise from normalization of neuroendocrine systems whose function has been distorted by chronic stress. Further randomized clinical trials are in progress with a focus on underserved minority populations.

ORIGINAL INVESTIGATION

Effects of a Randomized Controlled Trial of Transcendental Meditation on Components of the Metabolic Syndrome in Subjects With Coronary Heart Disease

Maura Paul-Labrador, MPH; Donna Polk, MD, MPH; James H. Dwyer, PhD†; Ivan Velasquez, MD; Sanford Nidich, PhD; Maxwell Rainforth, PhD; Robert Schneider, MD; C. Noel Bairey Merz, MD

Background: The metabolic syndrome is thought to be a contributor to coronary heart disease (CHD), and components of the syndrome have been identified as possible therapeutic targets. Previous data implicate neurohumoral activation related to psychosocial stress as a contributor to the metabolic syndrome. The aim of this study was to evaluate the efficacy of transcendental meditation (TM) on components of the metabolic syndrome and CHD.

Methods: We conducted a randomized, placebo-controlled clinical trial of 16 weeks of TM or active control treatment (health education), matched for frequency and time, at an academic medical center in a total of 103 subjects with stable CHD. Main outcome measures included blood pressure, lipoprotein profile, and insulin resistance determined by homeostasis model assessment (calculated as follows: [(fasting plasma glucose level [in milligrams per deciliter] × fasting plasma insulin level [in microunits per milliliter]) × 0.0552]/22.5); endothelial function measured by brachial artery reactivity testing; and cardiac autonomic system activity measured by heart rate variability.

Results: The TM group had beneficial changes (measured as mean ± SD) in adjusted systolic blood pressure (−3.4 ± 2.0 vs 2.8 ± 2.1 mm Hg; $P = .04$), insulin resistance (−0.75 ± 2.04 vs 0.52 ± 2.84; $P = .01$), and heart rate variability (0.10 ± 0.17 vs −0.50 ± 0.17 high-frequency power; $P = .07$) compared with the health education group, respectively. There was no effect of brachial artery reactivity testing.

Conclusions: Use of TM for 16 weeks in CHD patients improved blood pressure and insulin resistance components of the metabolic syndrome as well as cardiac autonomic nervous system tone compared with a control group receiving health education. These results suggest that TM may modulate the physiological response to stress and improve CHD risk factors, which may be a novel therapeutic target for the treatment of CHD.

Arch Intern Med. 2006;166:1218-1224

(REPRINTED) ARCH INTERN MED/VOL 166, JUNE 12, 2006

Published in final edited form as:
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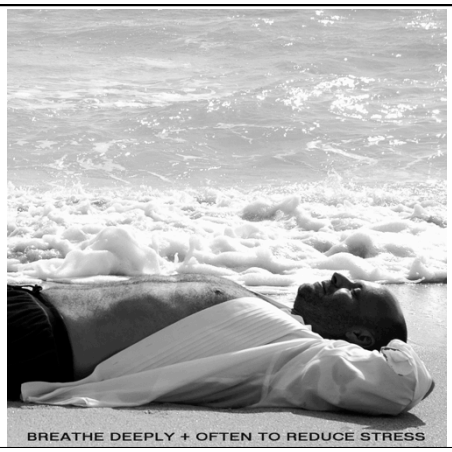

Aflibercept - Eylea

Intravitreal Aflibercept for Treatment-Resistant Neovascular Age-Related Macular Degeration

Ophthalmology
Vol 121 No.1 January 2014

Objective

To assess the effectiveness of intravitreal aflibercept in patients with neovascular age-related macular degeneration previously resistant to treatment with other anti-vascular endothelial frowth factor agents.

Intervention

A dose of 2mg intravitreal aflibercept was administered as 3 initial loading doses every 4 weeks, followed by further injections every 8 weeks across a 24-week period in total.

Main Outcome Measures

Outcomes assessed included proportions of patients with a gain or loss of more than 5 ETDRS letters and a decrease or increase in central retinal thickness of more than 150 um at week 24 compared with baseline, change in mean BCVA and CRT between baseline and week 24, and descriptive safety data.

Results

BCVA improved and CRT was reduced significantly at all follow-up visits compared with baseline ($P<0.0001$), with a mean improvement of 6.9 letters of BCVA and a decrease of 89.4um in CRT at week24. Spacing of injections from every 4 weeks to every 8 weeks resulted in an increase of 37.4um in CRT ($P<0.0001$); however, this was not correlated with a significant change in vision.

Conclusion

Intravitreal Aflibercept is effective in previously treatment-resistant Age-Related Macular Degeneration




FEEL
MORE
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