Shawn M. Talbott, PhD

CNS, LDN, FACSM, FAIS, FACN

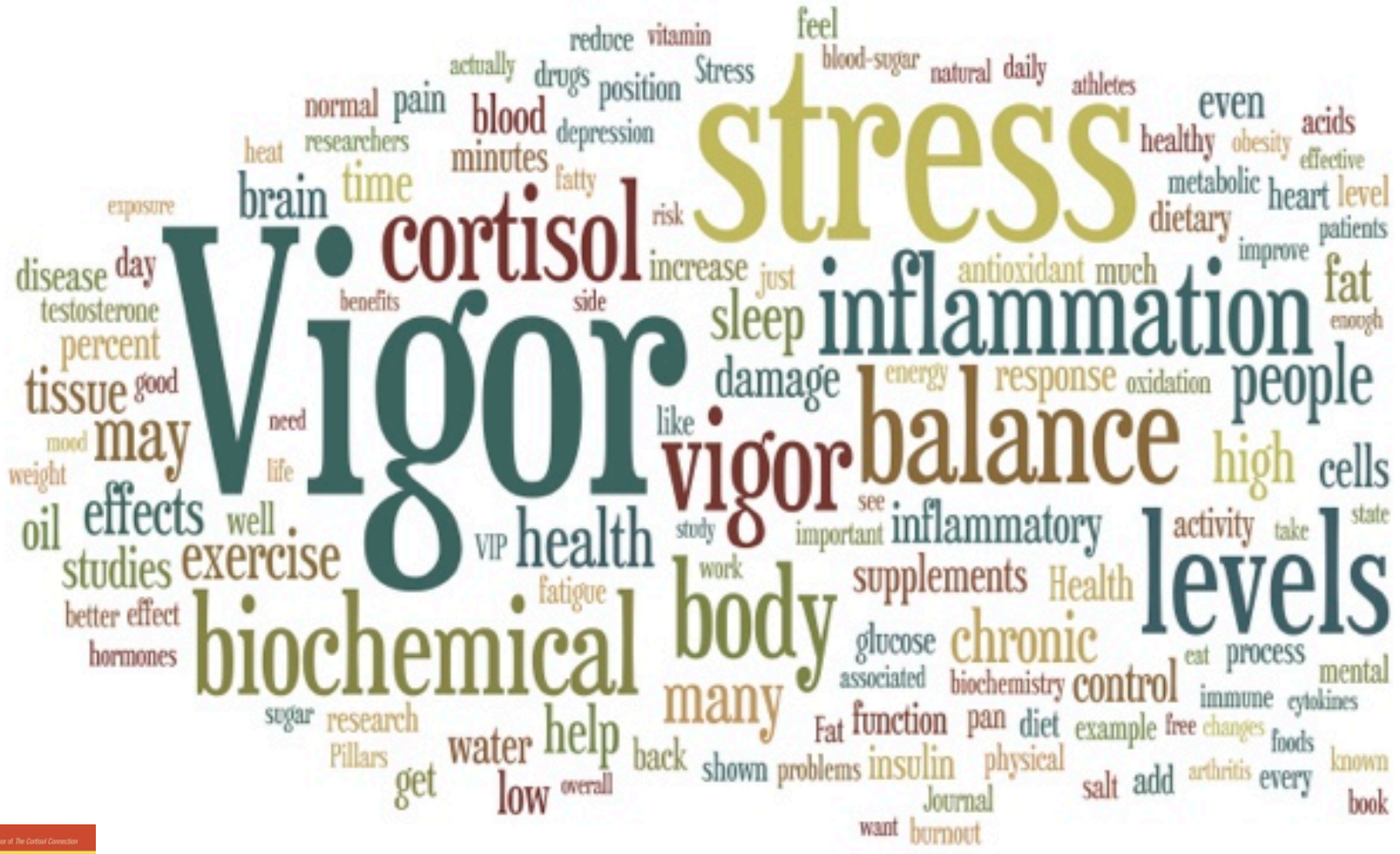
Chief Science Officer, LifeVantage

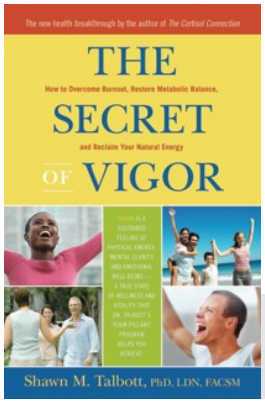
LifeVantage.

Vigor

3-tiered sustained mood state characterized by
physical energy, mental acuity, and emotional well-being

LifeVantage.





LifeVantage.

Diet / Vigor Relationship

- Mediterranean diet = Improved QOL
  - Henriquez-Sanchez et al. *Eur J Clin Nutr* 66(3): 360-8, 2012
- Omega3s = Reduced ADHD Sx / Improved QOL (cancer)
  - Van der Meij et al. *Eur J Clin Nutr* 66, 399-404, 2012
- Multivitamin = Increased Attention, Mood, Vigor
  - Kennedy et al. *Psychopharmacology* 211:55-68, 2010
- Overall Diet Quality = Reduced Depression / Improved QOL
  - Kuczmarski et al. *J Am Diet Assoc.* 110(3): 383-389, 2010
- Fast Food / Commercial baked Goods = Higher Depression Risk
  - Sanchez-Vilegas et al. *Public Health Nutr* 15(3), 424-432, 2011
- Food restriction (lightweight athletes) = Reduced Vigor
  - Filaire et al. *Int J Sports Med.* Aug;22(6):454-9. 2001
- Bonito (tuna) Broth (EAAs) = Reduced Fatigue / Improved Vigor
  - Kuroda & Nozawa. *Biomed Res* 29(4), 175-179, 2008
- Positive Psychological Well-Being = longer survival (healthy/diseased)
  - Chida & Steptoe. *Psychosomatic Med* 70:741-756, 2008

LifeVantage.

Prevalence of Chronic Stress

- Studies show that 50-60% of all lost working days are related to stress
- Work-related stress costs the EU more than 265 billion Euros annually
- Chronic stress is a determinant of Depression, Heart Disease, Diabetes, & Syndrome X
- Stress contributes to half of all illnesses in the United States
- 70-80% of all doctor visits are for stress-related illnesses
- More than half of all deaths before age 65 result from stressful lifestyles
- Generalized anxiety disorder affects ~183 million people worldwide
- People with high anxiety are 4.5x more likely to die of a heart attack or stroke
- 80% of workers report feeling stress on the job
- 65% = American Psychological Association
- 70-80% = World Health Organization (WHO) & Centers for Disease Control (CDC)
- 90% = American Institute of Stress (AIS)

Sources: Working on Stress - European Agency for Safety and Health at Work (http://agency.osha.eu.int)

U.S. Center for Disease Control

World Health Organization; www.whmc.af.mil

2000 Gallup Poll "Attitudes in the American Workplace"

LifeVantage.

Stress-Related Conditions

Metabolic and Long-Term Health Effects of Elevated Stress (Cortisol Overexposure/Metabolic Imbalance)

- Increased appetite, Accelerated muscle catabolism, Suppressed fat oxidation, Enhanced fat storage **(Obesity - 2,694)**
- Elevated cholesterol and triglyceride levels; Elevated blood pressure **(Heart disease - 4,604)**
- Alterations in brain neurochemistry [dopamine/serotonin/norepinephrine] **(Depression/Anxiety/ADHD - 22,491)**
- Physical atrophy of brain cells **(Memory problems/Dementia - 3,169)**
- Insulin resistance and elevated blood-sugar levels **(Diabetes - 1,203)**
- Accelerated bone resorption **(Osteoporosis - 2,675)**
- Reduced levels of testosterone **(Suppressed libido - 1,439)**
- Suppression of immune-cell number/activity **(Frequent Colds/Flu/infection; Increased Cancer risk - 9,651)**

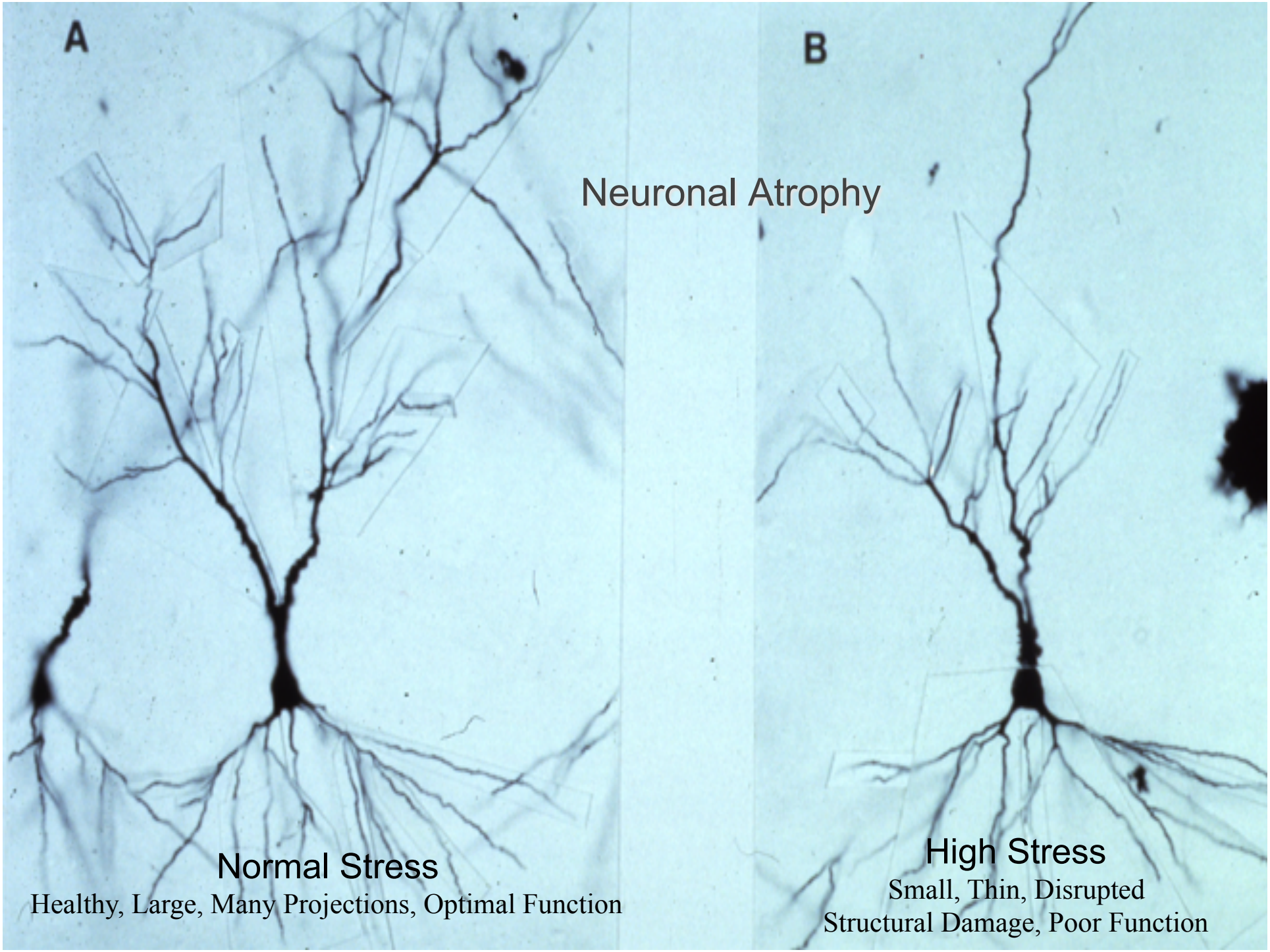
LifeVantage.

Causes of "Imbalance" (Stress)

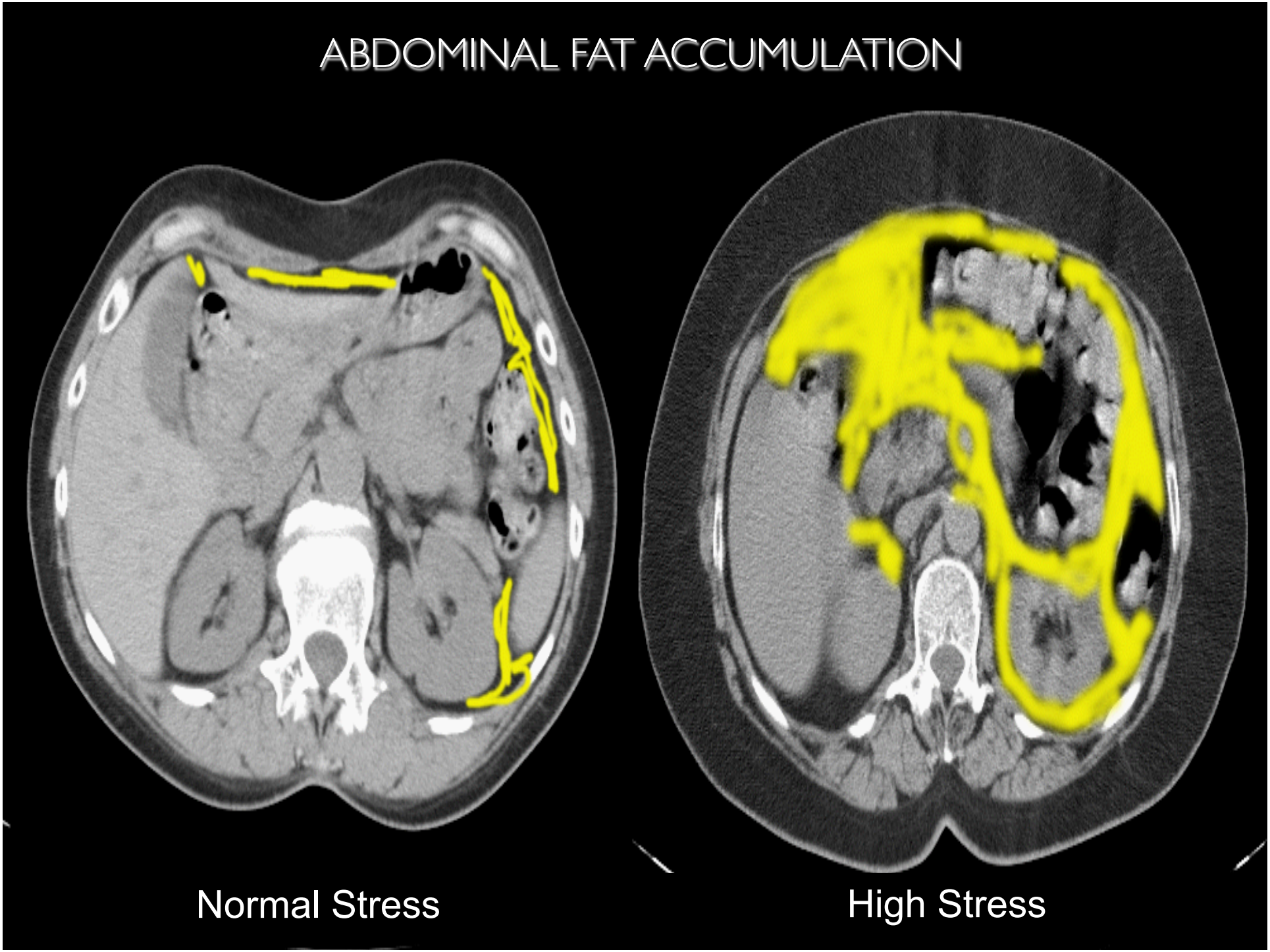
- Emotional stress (deadlines, bills, traffic…)
- Physical stress (aging, sleep deprivation, exercise…)
- Environmental stress (air/water pollution, heat, cold…)
- Non-Optimal Diet (processed foods, inadequate (phyto)nutrients…)
- Sources of Imbalance (stress) are:
  - Internal
  - External
  - Everywhere!
  - Unavoidable!!
- Athletes / Dieters / Short-Sleepers / Stressed
  - Share the SAME *biochemical* disruptions
  - Share the SAME *psychological* outcomes
  - Exhibit the SAME benefits to *restored biochemical balance*

LifeVantage

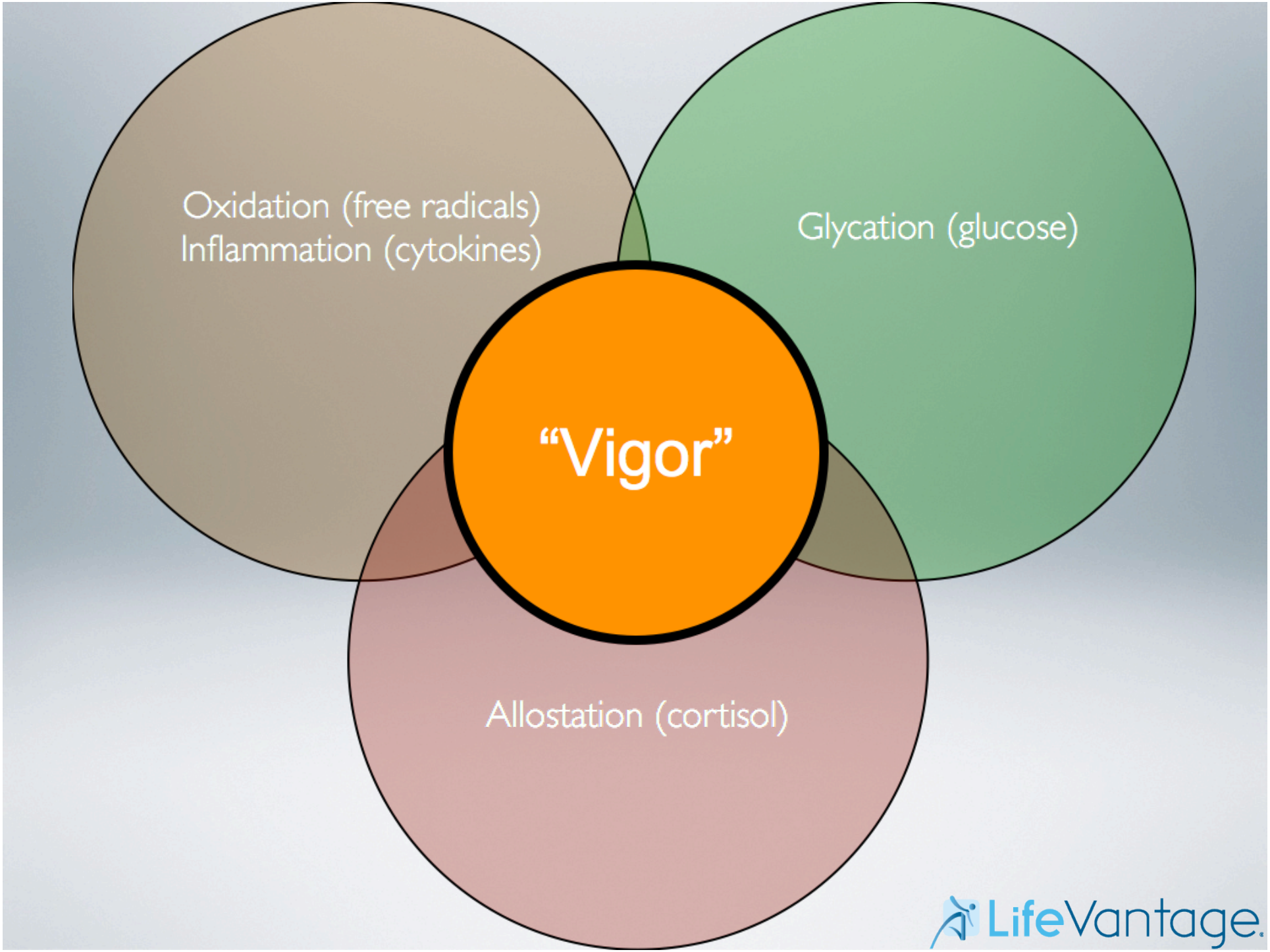

ADDERALL XR
PROZAC
PROVIGIL (MODAFINIL) Tablets
Lunesta
STARBUCKS COFFEE
Lexapro
MONSTER ENERGY
Folgers
Ritalin-SR
Celexa
Vyvanse
PAXIL
$100B+
Zoloft
Wellbutrin XL
strattera atomoxetine HCl
uvox
AMBIEN
ROCKSTAR ENERGY DRINK
EFFEXOR XR
CONCERTA
Cymbalta
Peets Coffee & Tea
DUNKIN' DONUTS
LifeVantage


A
B
Neuronal Atrophy
Normal Stress
Healthy, Large, Many Projections, Optimal Function
High Stress
Small, Thin, Disrupted
Structural Damage, Poor Function

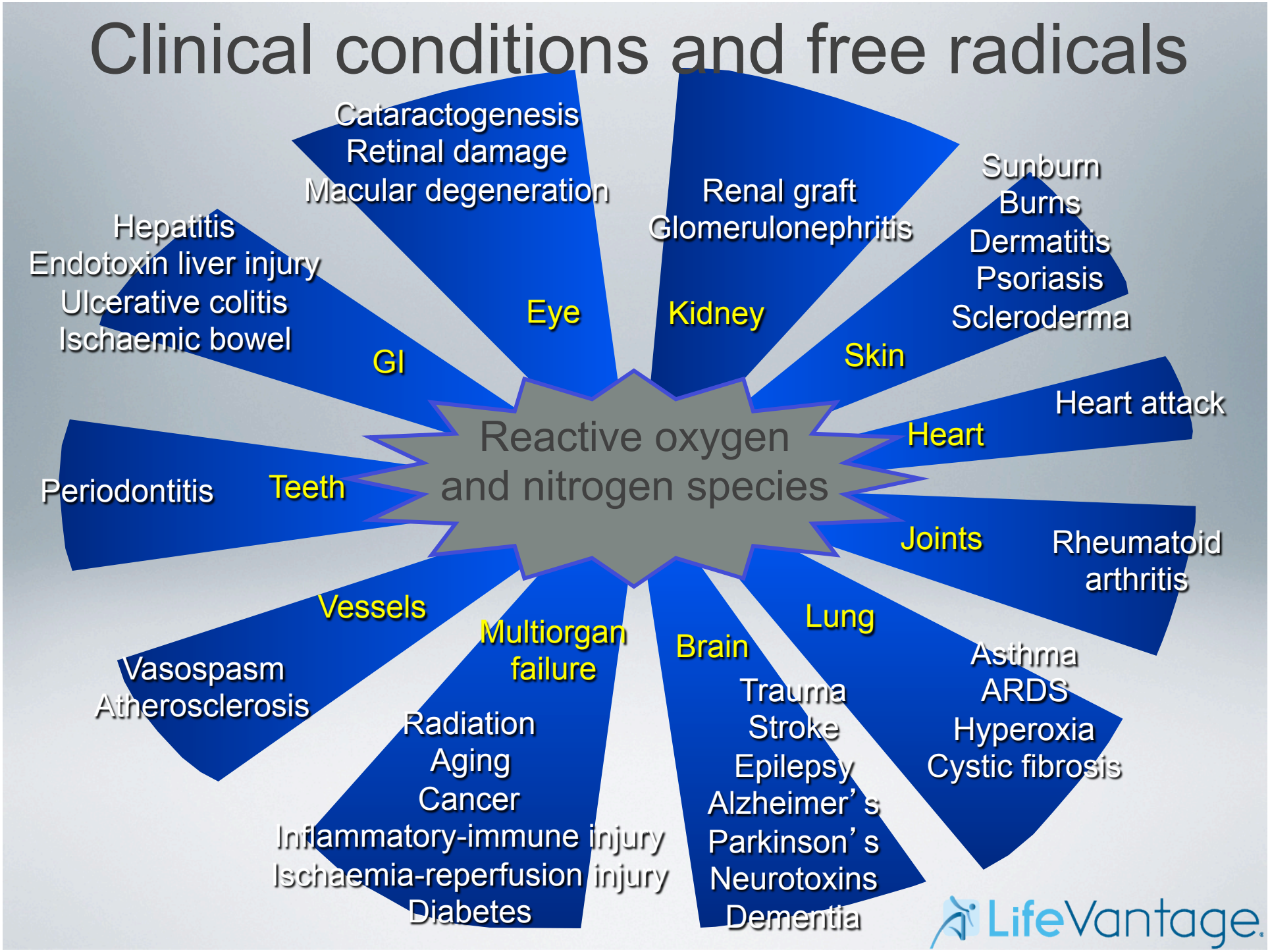
ABDOMINAL FAT ACCUMULATION



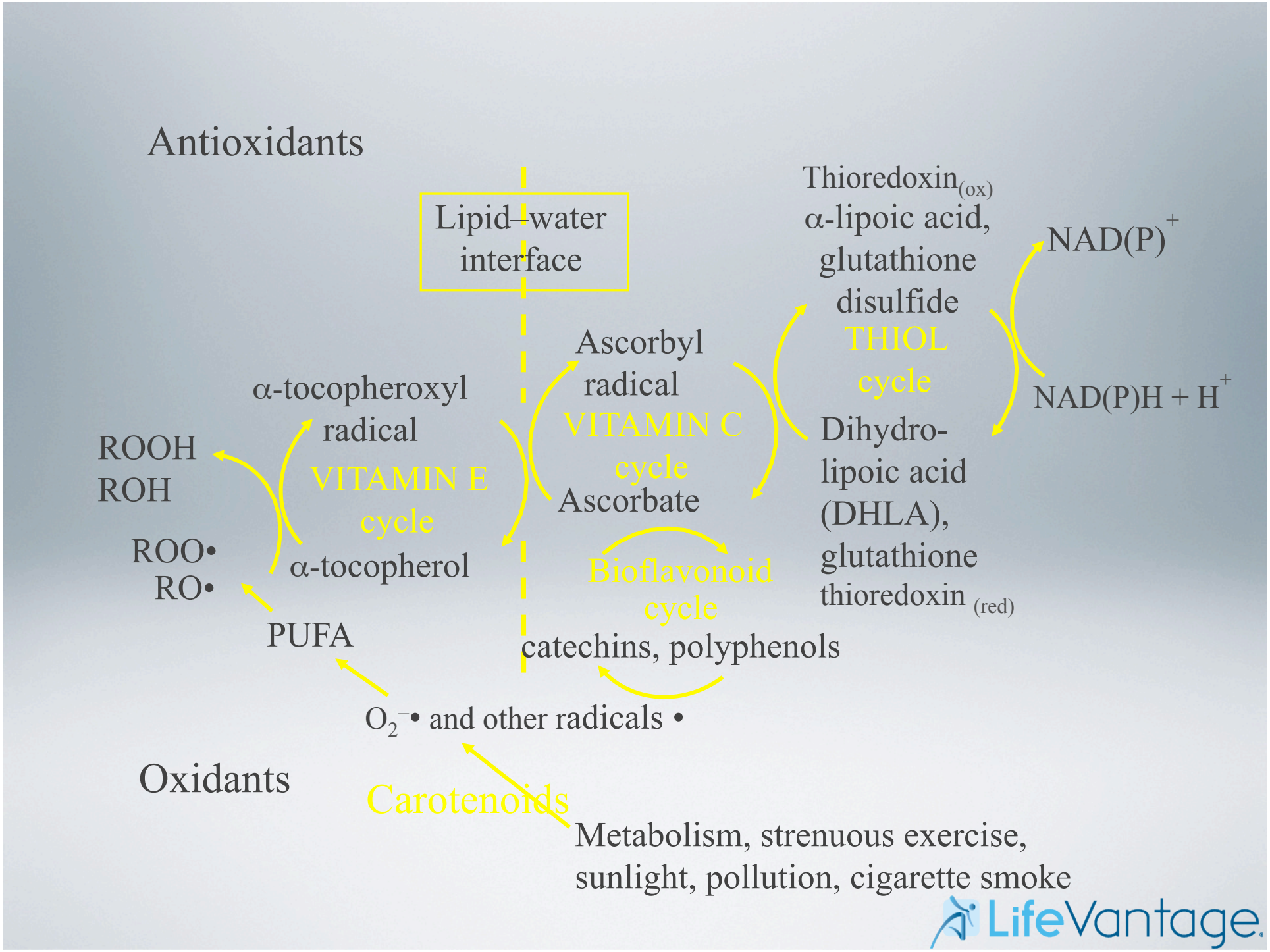
LifeVantage.


Oxidation (free radicals)
Inflammation (cytokines)
Glycation (glucose)
"Vigor"
Allostation (cortisol)
LifeVantage.

Clinical conditions and free radicals



LifeVantage


Antioxidants
Lipid–water interface
Thioredoxin(ox)
α-lipoic acid,
glutathione
disulfide
NAD(P)+
THIOL cycle
NAD(P)H + H+
Ascorbyl radical
VITAMIN C cycle
Ascorbate
Dihydro-lipoic acid (DHLA), glutathione thioredoxin (red)
α-tocopheroxyl radical
VITAMIN E cycle
α-tocopherol
ROOH
ROH
ROO•
RO•
PUFA
Bioflavonoid cycle
catechins, polyphenols
O2−• and other radicals •
Oxidants
Carotenoids
Metabolism, strenuous exercise,
sunlight, pollution, cigarette smoke
LifeVantage

ORIGINAL CONTRIBUTION

Vitamin E and the Risk of Prostate Cancer

The Selenium and Vitamin E Cancer Prevention Trial (SELECT)

Eric A. Klein, MD
Ian M. Thompson Jr, MD
Catherine M. Tangen, DrPH
John J. Crowley, PhD
M. Scott Lucia, MD
Phyllis J. Goodman, MS
Lori M. Minasian, MD
Leslie G. Ford, MD
Howard L. Parnes, MD
J. Michael Gaziano, MD, MP
Daniel D. Karp, MD
Michael M. Lieber, MD
Philip J. Walther, MD, PhD
Laurence Klotz, MD
J. Kellogg Parsons, MD, MH
Joseph L. Chin, MD
Amy K. Darke, MS
Scott M. Lippman, MD
Gary E. Goodman, MD
Frank L. Meyskens Jr, MD
Laurence H. Baker, DO

LIFETIME RISK OF PROS
cer in the United Sta
rently estimated to be
though most cases ar
an early, curable stage, tre
costly and urinary, sexual, a
related adverse effects are
Even men who choose activ
lance as an initial manager
egy face anxiety, uncertain
and a measurable risk of sepsi
low-up biopsies,[3] and more
third of those who initially de
are ultimately treated.[4,5] Wi

Author Video Interview ava
www.jama.com.

EFFECTS OF A COMBINATION OF BETA CAROTENE AND VITAMIN A CARDIOVASCULAR DISEASE

GILBERT S. OMENN, M.D., PH.D., GARY E. GOODMAN, M.D., M.S., MARK JOHN BALMES, M.D., MARK R. CULLEN, M.D., ANDREW GLASS, M.D., JA FRANK L. MEYSKENS, JR., M.D., BARBARA VALANIS, DR.P.H., JAMES H. SCOTT BARNHART, M.D., M.P.H., AND SAMUEL HAMMAR,

Abstract *Background.* Lung cancer and cardiovascular disease are major causes of death in the United States. It has been proposed that carotenoids and retinoids are agents that may prevent these disorders.

Methods. We conducted a multicenter, randomized, double-blind, placebo-controlled primary prevention trial — the Beta-Carotene and Retinol Efficacy Trial — involving a total of 18,314 smokers, former smokers, and workers exposed to asbestos. The effects of a combination of 30 mg of beta carotene per day and 25,000 IU of retinol (vitamin A) in the form of palmitate per day on the primary end point, the incidence of lung cancer, were compared with those of placebo.

Results. A total of 388 new cases of lung cancer were diagnosed during the 73,135 person-years of follow-up (mean length of follow-up, 4.0 years). The active-treatment group had a relative risk of lung cancer of 1.28 (95 percent confidence interval, 1.04 to 1.57; P = 0.02), as compared with the placebo group. There were also significantly different

LUNG cancer is the leading cause of death from cancer in the United States, accounting for approximately 29 percent of deaths from cancer and 6 percent of all deaths.[1] New approaches are essential to prevent lung cancer in persons who have smoked cigarettes or who have had occupational exposure to asbestos. Twenty-nine percent of men and 25 percent of women who are 45 to 64 years of age currently smoke,[2] and at least 40 percent of men and 20 percent of women in this age group are former smokers.[3] An estimated 4000 to 6000 deaths from lung cancer per year are attributed to exposure to asbestos.[4,5]

On the basis of epidemiologic observations and laboratory studies, beta carotene and vitamin A have attracted wide interest as agents that may prevent lung cancer.[6,7] The Beta-Carotene and Retinol Efficacy Trial (CARET) is one of several recent trials to assess the chemopreventive efficac
and related agents.[8-13]

This report presents
CARET study, which coi
of the steering committee
to stop the trial's active
ditional end points is ex
five years.

Study Design

The study's strategy, desig
study findings, and recruitment
where.[8,9,14] Briefly, CARET w
domization in Seattle in 1985
men with substantial occupati
randomly assigned in a 1:1 ra
15 mg of beta carotene per da
tive treatment) or placebo; the
with extensive histories of ciga
carotene per day, 25,000 IU of
ther vitamin (two-by-two desig
additional study centers in 198
domly assigned in a 1:1 ratio
The pilot groups receiving active agents were consolidated
into a single group receiving a standard daily regimen of
beta carotene plus 25,000 IU of retinol in the form of retin
tate. Thus, in the pilot study with the cohort of smokers, t
jects were assigned to active treatment for every subject as
placebo; therefore, the rates rather than numbers of end po
be compared between active and placebo groups. The desig
for active intervention until late 1997 (110,000 person-years)
porting of results in 1998.

Eligibility, Recruitment, and Randomization

Workers exposed to asbestos were men 45 to 74 years
the pilot study and 45 to 69 years of age in the later peri

From the Division of Public Health Sciences, Fred Hutchinson Cancer Research Center, Seattle (G.S.O., G.E.G., M.D.T., S.B.); the Departments of Environmental Health and Medicine, University of Washington, Seattle (G.S.O., G.E.G., S.B., S.H.); the Swedish Hospital Tumor Institute, Seattle (G.E.G.); the Department of Medicine, University of California at San Francisco, San Francisco (J.B.); the Department of Medicine, Yale University, New Haven, Conn. (M.R.C.); Kaiser Permanente Center for Health Research, Portland, Oreg. (A.G., B.V.); the Department of Medicine, University of Maryland, Baltimore (J.P.K.); and the Department of Medicine and Cancer Center, University of California at Irvine, Orange (F.L.M., J.H.W.). Address reprint requests to Dr. Omenn at the Fred Hutchinson Cancer Research Center, Division of Public Health Sciences, 1124 Columbia–MP859, Seattle, WA 98104.

Supported by grants (U01 CA63673, U01 CA63674, U01 CA47989, U01 CA48200, U01 CA48201, U01 CA48196, and U01 CA52596) from the National Cancer Institute.

*Other contributing authors were Carl Andrew Brodkin, M.D. (University of Washington, Seattle), Martin G. Cherniack, M.D. (Yale University, New Haven, Conn.), James E. Grizzle, Ph.D. (Fred Hutchinson Cancer Research Center, Seattle), Marjorie Perloff, M.D. (National Cancer Institute, Bethesda, Md.), and Linda Rosenstock, M.D., M.P.H. (University of Washington, Seattle).

α-Tocopherol and β-Carotene Supplements and Lung Cancer Incidence in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study: Effects of Base-line Characteristics and Study Compliance

*Demetrius Albanes, Olli P. Heinonen, Philip R. Taylor, Jarmo Virtamo, Brenda K. Edwards, Matti Rautalahti, Anne M. Hartman, Juni Palmgren, Laurence S. Freedman, Jaason Haapakoski, Michael J. Barrett, Pirjo Pietinen, Nea Malila, Eero Tala, Kari Liippo, Eija-Riitta Salomaa, Joseph A. Tangrea, Lyly Teppo, Frederic B. Askin, Eero Taskinen, Yener Erozan, Peter Greenwald, Jussi K. Huttunen**

Background *suggest that of vitamin E other foods precursor o dark-green, the risk of c ings of th Prevention lung cancer who receive were recentl ficacy Trial carotene an of α-tocoph cidence of l the ATBC age, numbe status, and in relation t tologic typ whether the could facili Study result tion and r total of 29 or more c receive α-t tocopherol (median, 6.1 factors for l study entry, tocopherol = 894) were and death c pendently c able for 9 evaluated h hazards mo*

THE JOURNAL OF NUTRITION JN

The Journal of Nutrition
Nutritional Epidemiology

Antioxidant Supplementation Increases the Risk of Skin Cancers in Women but Not in Men[1]

Serge Hercberg,[2,3]* Khaled Ezzedine,[2,4] Christiane Guinot,[5,6] Paul Preziosi,[2] Pilar Galan,[2] Sandrine Bertrais,[2] Carla Estaquio,[2] Serge Briançon,[7] Alain Favier,[8] Julie Latreille,[5] and Denis Malvy[9]

[2]UMR U557 Inserm/U1125 Inra/EA3200 Cnam/Univ Paris 13, Bobigny, France 93017; [3]Unité de Surveillance et d'Epidémiologie Nutritionnelle; Centre de Recherche en Nutrition Humaine Ile-de-France UFR SMBH Paris 13, Bobigny, France 93017; [4]Department of Dermatology, University Hospital Erasme, Université Libre de Bruxelles, Bruxelles, Belgium 1070; [5]Biometrics and Epidemiology Unit, CE.R.I.E.S., Neuilly sur Seine, France 92521; [6]Computer Science Laboratory, Ecole Polytechnique, Université de Tours, Tours, France 37200, [7]EA 3444, Ecole de Santé Publique, Epidémiologie clinique, Faculté de Médecine, CHU Nancy, France 54035; [8]Laboratoire Lésions des Acides Nucléiques, UMR CNRS-CEA-UJF 5046, Grenoble, France 38000; and [9]EA 3677 and Centre René-Labusquière (Tropical Medicine and International Health Branch), Université Victor Segalen Bordeaux 2 and Department of Internal Medicine and Tropical Diseases, University Hospital Center, Bordeaux, France 33076

Abstract

This research aimed to test whether supplementation with a combination of antioxidant vitamins and minerals could reduce the risk of skin cancers (SC). It was performed within the framework of the Supplementation in Vitamins and Mineral Antioxidants study, a randomized, double-blinded, placebo-controlled, primary prevention trial testing the efficacy of nutritional doses of antioxidants in reducing incidence of cancer and ischemic heart disease in the general population. French adults (7876 women and 5141 men) were randomized to take an oral daily capsule of antioxidants (120 mg vitamin C, 30 mg vitamin E, 6 mg β-carotene, 100 μg selenium, and 20 mg zinc) or a matching placebo. The median time of follow-up was 7.5 y. A total of 157 cases of all types of SC were reported, from which 26 were melanomas. Because the effect of antioxidants on SC incidence varied according to gender, men and women were analyzed separately. In women, the incidence of SC was higher in the antioxidant group [adjusted hazard ratio (adjusted HR) = 1.68; $P = 0.03$]. Conversely, in men, incidence did not differ between the 2 treatment groups (adjusted HR = 0.69; $P = 0.11$). Despite the small number of events, the incidence of melanoma was also higher in the antioxidant group for women (adjusted HR = 4.31; $P = 0.02$). The incidence of nonmelanoma SC did not differ between the antioxidant and placebo groups (adjusted HR = 1.37; $P = 0.22$ for women and adjusted HR = 0.72; $P = 0.19$ for men). Our findings suggest that antioxidant supplementation affects the incidence of SC differentially in men and women. J. Nutr. 137: 2098–2106, 2007.

Introduction

Melanoma and nonmelanoma skin cancers (SC),[10] namely squamous cell carcinoma (SCC) and basal cell carcinoma (BCC), are the most common forms of malignancy in the Caucasian population (1) and sun exposure is thought to be the main established risk factor for all 3 types of tumor (2). An aging population, more intense exposure to UV rays due to depletion of the ozone layer, and sun exposure habits would appear to favor a higher incidence of skin malignancy (3).

Numerous studies have demonstrated the role of reactive oxygen species, also called free radicals, in skin carcinogenesis and the potential protective effect of antioxidants (4). Formation of free radicals in the skin can be enhanced by UV r
cutaneous system has a very efficient interlinked
defense system for counteracting UV-induced oxi
However, excessive exposure to sunlight or other s
light can overwhelm the skin's antioxidant capacity. A potentially interesting strategy for preventing UV exposure damage could be to boost the endogenous antioxidant system by oral intake of antioxidant vitamins and minerals. Although clinical trials have showed contradictory findings (5–7), oral antioxidant pills have been recommended for the prevention of sunburns and for their supposed photoprotective properties.

In particular, it has been suggested that nutrients such as β-carotene, ascorbic acid, vitamin E, selenium, and zinc may prevent such harmful effects of UV exposure because of their antioxidant ability (8). Clinical trials testing the impact of supplementation with high doses of antioxidants over long periods have, however, failed to reveal beneficial effects on the incidence of SC (9,10). For example, the Nutritional Prevention of Cancer trial, a double-blind, randomized clinical trial, was designed to test whether selenium (200 μg/d) could prevent nonmelanoma SC (NMSC) in 1312 individuals with an individual

[1] Author disclosures: S. Hercberg, K. Ezzedine, P. Preziosi, P. Galan, S. Bertrais, C. Estaquio, S. Briançon, A. Favier, and D. Malvy, no conflicts of interest; C. Guinot and J. Latreille, the CE.R.I.E.S. is a research center on human skin founded by CHANEL.

[2] Abbreviations used: BCC, basal cell carcinoma; HR, hazard ratio; MSC, melanoma skin cancer; NMSC, nonmelanoma skin cancer; SC, skin cancer; SCC, squamous cell carcinoma; SU.VI.MAX, Supplémentation en Vitamines et Minéraux Antioxydants study.

* To whom correspondence should be addressed. E-mail: hercberg@cnam.fr.

0022-3166/07 $8.00 © 2007 American Society for Nutrition.
Manuscript received 28 February 2007. Initial review completed 21 March 2007. Revision accepted 22 June 2007.

Text

Annals of Internal Medicine NIH CONFERENCE

The Efficacy and Safety of Multivitamin and Mineral Supplement Use To Prevent Cancer and Chronic Disease in Adults: A Systematic Review for a National Institutes of Health State-of-the-Science Conference

Han-Yao Huang, PhD, MPH; Benjamin Caballero, MD, PhD; Stephanie Chang, MD; Anthony J. Alberg, PhD, MPH; Richard D. Semba, MD, MPH; Christine R. Schneyer, MD; Renee F. Wilson, MSc; Ting-Yuan Cheng, MSc; Jason Vassy, MPH; Gregory Prokopowicz, MD, MPH; George J. Barnes II, BA; and Eric B. Bass, MD, MPH

Background: Multivitamin and mineral supplements are the most commonly used dietary supplements in the United States.

Purpose: To synthesize studies on the efficacy and safety of multivitamin/mineral supplement use in primary prevention of cancer and chronic

Data Sourc EMBASE, a hand-searc

Study Sele viewed to observation safety.

Data Extra dently asse

Data Synth that assesse trials and 3 quality was disease, cat for the stu population, erol, and se

gastric cancer and the overall mortality rate from cancer by 13% to 21%. In a French trial, combined supplementation with vitamin C, vitamin E, β-carotene, selenium, and zinc reduced the rate of cancer by 31% in men but not in women. Multivitamin and mineral supplements had no significant effect on cardiovascular disease

Multi
con
States (1).
Examinati
recent use
use multiv
quate inta
monly us
supplemer
Many
cluding ci
style, and
these facto
damage, i

Annals
372 | 5 Septem

ORIGINAL INVESTIGATION

LESS IS MORE

Dietary Supplements and Mortality Rate in Older Women

The Iowa Women's Health Study

Jaakko Mursu, PhD; Kim Robien, PhD; Lisa J. Harnack, DrPH, MPH; Kyong Park, PhD; David R. Jacobs Jr, PhD

Background: Although dietary supplements are commonly taken to prevent chronic disease, the long-term health consequences of many compounds are unknown.

Methods: We assessed the use of vitamin and mineral supplements in relation to total mortality in 38 772 older women in the Iowa Women's Health Study; mean age was 61.6 years at baseline in 1986. Supplement use was self-reported in 1986, 1997, and 2004. Through December 31, 2008, a total of 15 594 deaths (40.2%) were identified through the State Health Registry of Iowa and the National Death Index.

Results: In multivariable adjusted proportional hazards regression models, the use of multivitamins (hazard ratio, 1.06; 95% CI, 1.02-1.10; absolute risk increase, 2.4%), vitamin B_6 (1.10; 1.01-1.21; 4.1%), folic acid (1.15; 1.00-1.32; 5.9%), iron (1.10; 1.03-1.17; 3.9%), magnesium (1.08; 1.01-1.15; 3.6%), zinc (1.08; 1.01-1.15; 3.0%), and copper (1.45; 1.20-1.75; 18.0%) were associated with increased risk of total mortality when compared with corresponding nonuse. Use of calcium was inversely related (hazard ratio, 0.91; 95% confidence interval, 0.88-0.94; absolute risk reduction, 3.8%). Findings for iron and calcium were replicated in separate, shorter-term analyses (10-year, 6-year, and 4-year follow-up), each with approximately 15% of the original participants having died, starting in 1986, 1997, and 2004.

Conclusions: In older women, several commonly used dietary vitamin and mineral supplements may be associated with increased total mortality risk; this association is strongest with supplemental iron. In contrast to the findings of many studies, calcium is associated with decreased risk.

Arch Intern Med. 2011;171(18):1625-1633

Author Affiliations: Department of Health Sciences, Institute of Public Health and Clinical Nutrition, University of Eastern Finland, Kuopio Campus, Kuopio, Finland (Dr Mursu); Division of Epidemiology and Community Health, School of Public Health, University of Minnesota, Minneapolis (Drs Mursu, Robien, Harnack, and Jacobs); Department of Food and Nutrition, Yeungnam University, Gyeongbuk, Republic of Korea (Dr Park); and Department of Nutrition, School of Medicine, University of Oslo, Oslo, Norway (Dr Jacobs).

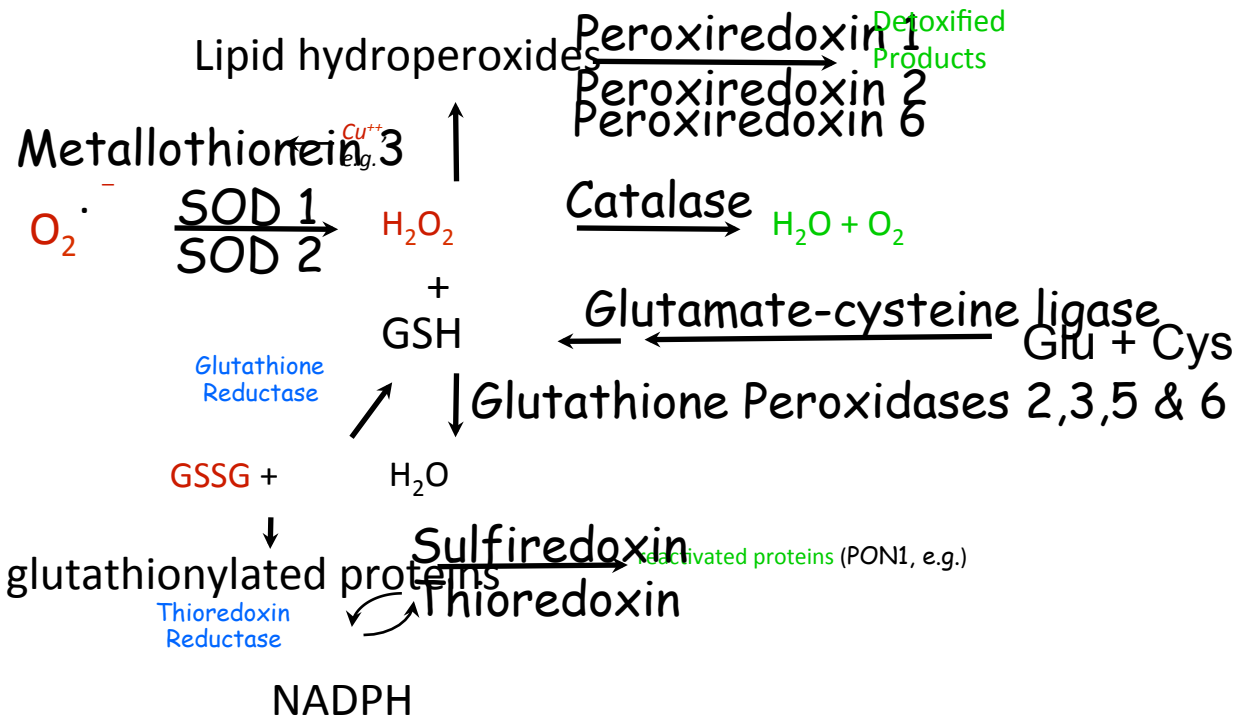
IN THE UNITED STATES, THE USE OF dietary supplements has increased substantially during the past several decades,[1-3] reaching approximately one-half of adults in 2000, with annual sales of more than $20 billion.[1-3] Sixty-six percent of women participating in the Iowa Women's Health Study[2] used at least 1 dietary supplement daily in 1986 at an average age of 62 years; in 2004, the proportion increased to 85%. Moreover, 27% of women reported using 4 or more supplemental products in 2004.[2] At the population level, dietary supplements contributed substantially to the total intake of several nutrients, particularly in elderly individuals.[1,2]

Supplemental nutrient intake clearly is beneficial in deficiency conditions.[3] However, in well-nourished populations, supplements often are intended to yield benefit by preventing chronic diseases. Results of epidemiologic studies[3-9] assessing supplement use and total mortality risk have been inconsistent. Several randomized controlled trials (RCTs),[10,11] concentrating mainly on calcium and vitamins B, C, D, and E, have not shown beneficial effects of

See Invited Commentary and Editor's Note at end of article

dietary supplements on total mortality rate; in contrast, some[12,13] have suggested the possibility of harm. Meta-analyses[14,15] concur in finding no decreased risk and potential harm. Supplements are widely used, and further studies regarding their health effects are needed. Also, little is known about the long-term effects of multivitamin use and less commonly used supplements, such as iron and other minerals.

The Internal System of Protective Antioxidant Enzymes



LifeVantage

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION
Heart Failure

Chronic Pulmonary Artery Pressure Elevation Is Insufficient to Explain Right Heart Failure

Harm J. Bogaard. MD. PhD*: Ramesh Nataraian. PhD*: Scott C. Henderson. PhD: Carlin

Background— function, bt of data on t
Methods and banding, nc angiopoiiti hypertroph that was as endothelial factor-1α. I (Protandim;
Conclusion— hypertensio
Ke

ELSEVIER journal home

Original Contribution

Protandim attenuates intimal ex vivo via a catalase-depend

Binata Joddar [a,b,c], Rashmeet K. Reen [b] Jay L. Zweier [b], Keith J. Gooch [a,b,*]

[a] Department of Biomedical Engineering, The Ohio State Univers
[b] Davis Heart & Lung Research Institute, The Ohio State Univers
[c] RIKEN Nanomedical Engineering Laboratory, Wako-shi, Saitam
[d] Department of Surgery, The Ohio State University, Columbus, (
[e] Department of Cardiothoracic Surgery, The Ohio State Universi
[f] Division of Pulmonary and Critical Care Medicine, Department

ARTICLE INFO

Article history:
Received 26 August 2010
Revised 7 December 2010
Accepted 8 December 2010
Available online 15 December 2010

Keywords:
Free radicals
Scavenging enzymes
Catalase
Human saphenous veins
Ex vivo culture
Protandim

AB

Huma
patency. To evaluate the role of reactive oxygen species (ROS) signaling in intima hyperplasia (IH), an early stage pathology of vein-graft disease, and to explore the potential therapeutic effects of up-regulating endogenous antio
model of HSV IH.
~3.6-fold increase
Protandim, a nutr
enzymes in severa
isolated HSV. Prot
respectively, and d
catalase activity by
and proliferation.
cultured HSV and

The Dietary Supplem
Plasma Osteopontin a
Oxidative Stress in Mus

Muhammad Mudda
Warren C. McClure, MS
Nicole L. Arevalo, MA
Rick E. Rabon, BA
Benjamin Mohr
Swapan K. Bose, BS, BPharm
Joe M. McCord, PhD
Brian S. Tseng, MD, PhD

ABSTRACT. Therapeutic options for Duchenne muscular dystrophy (DMD), t common and lethal neuromuscular disorder in children, remain elusive. O damage is implicated as a pertinent factor involved in its pathogenesis. Protan an over-the-counter supplement with the ability to induce antioxidant enzymes

US007241

(12) United States Patent
Myhill et al.

(10) Patent No.:
(45) Date of Patent:

(54) COMPOSITIONS FOR ALLEVIATING INFLAMMATION AND OXIDATIVE STRESS IN A MAMMAL

(75) Inventors: Paul R. Myhill, Castle Rock, CO (US); William J. Driscoll, Englewood, CO (US)

(73) Assignee: Lifeline Nutraceuticals Corporation, Englewood, CO (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: 11/088,323

(22) Filed: Mar. 23, 2005

(65) Prior Publication Data

US 2005/0226942 A1 Oct. 13, 2005

Related U.S. Application Data

(60) Provisional application No. 60/646,707, filed on Jan. 25, 2005, provisional application No. 60/643,754, filed on Jan. 13, 2005, provisional application No. 60/610,749, filed on Sep. 17, 2004, provisional appli-

Al-Shaer, "C-Reactive Protein and 2004; vol. 291, No. 23: pp. 2818-2
Anderson, et al., "Differential Resp Cells to Induction of Apoptosis by V E Analogue, α-TEA," *Cancer Res.*,
Baker, et al., "Reduced RBC Versu Due to Endotoxin," *Circul. Shock*,
Barbosa, et al., "Decreased Oxidati ative Colitis Supplemented with Fi *tion*, 2003; vol. 19: pp. 837-842.
Bhattacharya, et al., "Antioxidant from *Withania somnifera*," *Ind. J. Exper. Biol.*, 1997; vol. 35: pp. 236-239.
Bhattacharya, et al., "Antioxidant Activity of *Bacopa monniera* in Rat Frontal Cortex, Striatum and Hippocampus," *Phytother. Res.*, 2000; vol. 14: pp. 174-179.
Bogarty, et al., "Biological Profiles in Subjects with Recurrent Acute Coronary Events Compared with Subjects with Long-standing Stable Angina," *Circulation*, 2001; vol. 103: pp. 3062-3068.
Bolibar, et al., "Short-term Prognostic Value of Lipid Measurements in Patients with Angina Pectoris," *Thromb. Haemost.*, 2000; vol. 84: pp. 955-960.
Bose, et al., "Membrane Lipid Peroxidation by UV-A: Mechanism and Implications," *Biotech. App. Biochem.*, 1990; vol. 12: pp. 557-561.
Boyd-Kimball, et al., "Rodent Aβ(1-42) Exhibits Oxidative Stress Properties Similar to Those of Human Aβ(1-42): Implications for Proposed Mechanisms of Toxicity," *J. Alzh. Dis.*, 2004; pp. 515-525.
Bridi, et al., "The Antioxidant Activity of Standardized Extract of *Ginkgo biloba* (EGb 761) in Rats," *Phytother. Res.*, 2001; vol. 15:

OPEN ACCESS Freely available online PLoS one

Protandim, a Fundamentally New Antioxidant Approach in Chemoprevention Using Mouse Two-Stage Skin Carcinogenesis as a Model

Jianfeng Liu[1], Xin Gu[2], Delira Robbins[1], Guohong Li[3], Runhua Shi[4], Joe M. McCord[5], Yunfeng Zhao[1]*

1 Department of Pharmacology, Toxicology & Neuroscience, Louisiana State University Health Sciences Center, Shreveport, Louisiana, United States of America, 2 Department of Pathology, Louisiana State University Health Sciences Center, Shreveport, Louisiana, United States of America, 3 Department of Neurosurgery, Louisiana State University Health Sciences Center, Shreveport, Louisiana, United States of America, 4 Feist-Weiller Cancer Center, Louisiana State University Health Sciences Center, Shreveport, Louisiana, United States of America, 5 Department of Medicine, University of Colorado Health Sciences Center, Denver, Colorado, United States of America

Abstract

Oxidative stress is an important contributor to cancer development. Consistent with that, antioxidant enzymes have been demonstrated to suppress tumorigenesis when being elevated both in vitro and in vivo, making induction of these enzymes a more potent approach for cancer prevention. Protandim, a well-defined combination of widely studied medicinal plants, has been shown to induce superoxide dismutase (SOD) and catalase activities and reduce superoxide generation and lipid peroxidation in healthy human subjects. To investigate whether Protandim can suppress tumor formation by a dietary approach, a two-stage mouse skin carcinogenesis study was performed. At the end of the study, the mice on a Protandim-containing basal diet had similar body weight compared with those on the basal diet, which indicated no overt toxicity by Protandim. After three weeks on the diets, there was a significant increase in the expression levels of SOD and catalase, in addition to the increases in SOD activities. Importantly, at the end of the carcinogenesis study, both skin tumor incidence and multiplicity were reduced in the mice on the Protandim diet by 33% and 57% respectively, compared with those on basal diet. Biochemical and histological studies revealed that the Protandim diet suppressed tumor promoter-induced oxidative stress (evidenced by reduction of protein carbonyl levels), cell proliferation (evidenced by reduction of skin hyperplasia and suppression of PKC/JNK/Jun pathway), and inflammation (evidenced by reduction of ICAM-1/VCAM-1 expression, NF-κB binding activity, and nuclear p65:p50 levels). Overall, induction of antioxidant enzymes by Protandim may serve as a practical and potent approach for cancer prevention.

Journal of the American College of Cardiology
© 2004 by the American College of Cardiology Foundation
Published by Elsevier Inc.
Vol
ISSN 07
doi:10.1016

Serum Levels of Thiobarbituric Acid Reactive Substances Predict Cardiovascular Events in Patients With Stable Coronary Artery Disease

A Longitudinal Analysis of the PREVENT Study

Mary F. Walter, PhD,* Robert F. Jacob, PhD,* Barrett Jeffers, PhD,† Mathieu M. Ghadanfar, M. Gregory M. Preston, PhD,§ Jan Buch, MD,† R. Preston Mason, PhD*†

Beverly and Boston, Massachusetts; New York, New York; and Groton, Connecticut

OPEN ACCESS Freely available online PLoS one

The Chemopreventive Effects of Protandim: Modulation of p53 Mitochondrial Translocation and Apoptosis during Skin Carcinogenesis

Delira Robbins[1], Xin Gu[2], Runhua Shi[6], Jianfeng Liu[1], Fei Wang[3], Jacqulyne Ponville[4], Joe M. McCord[5], Yunfeng Zhao[1]*

1 Department of Pharmacology, Toxicology and Neuroscience, Louisiana State University Health Sciences Center, Shreveport, Louisiana, United States of America, 2 Department of Pathology, Louisiana State University Health Sciences Center, Shreveport, Louisiana, United States of America, 3 College of Life Science, Jilin University, Changchun, Jilin Province, China, 4 Department of Chemistry, Nicholls State University, Thibodaux, Louisiana, United States of America, 5 Department of Medicine, University of Colorado at Denver and Health Sciences Center, Aurora, Colorado, United States of America, 6 Feist-Weiller Cancer Center, Louisiana State University Health Sciences Center, Shreveport, Louisiana, United States of America

Abstract

Protandim, a well defined dietary combination of 5 well-established medicinal plants, is known to induce endogenous antioxidant enzymes, such as manganese superoxide dismutase (MnSOD). Our previous studies have shown through the induction of various antioxidant enzymes, products of oxidative damage can be decreased. In addition, we have shown that tumor multiplicity and incidence can be decreased through the dietary administration of Protandim in the two-stage skin carcinogenesis mouse model. It has been demonstrated that cell proliferation is accommodated by cell death during DMBA/TPA treatment in the two-stage skin carcinogenesis model. Therefore, we investigated the effects of the Protandim diet on apoptosis; and proposed a novel mechanism of chemoprevention utilized by the Protandim dietary combination. Interestingly, Protandim suppressed DMBA/TPA induced cutaneous apoptosis. Recently, more attention has been focused on transcription-independent mechanisms of the tumor suppressor, p53, that mediate apoptosis. It is known that cytoplasmic p53 rapidly translocates to the mitochondria in response to pro-apoptotic stress. Our results showed that Protandim suppressed the mitochondrial translocation of p53 and mitochondrial outer membrane proteins such as Bax. We examined the levels of p53 and MnSOD expression/activity in murine skin JB6 promotion sensitive (P+) and promotion-resistant (P-) epidermal cells. Interestingly, p53 was induced only in P+ cells, not P- cells; whereas MnSOD is highly expressed in P- cells when compared to P+ cells. In addition, wild-type p53 was transfected into JB6 P- cells. We found that the introduction of wild-type p53 promoted transformation in JB6 P- cells. Our results suggest that suppression of p53 and induction of MnSOD may play an important role in the tumor suppressive activity of Protandim.

Contents lists available at ScienceDirect
Free Radical Biology & Medicine
journal homepage: www.elsevier.com/locate/freeradbiomed

Original Contribution

Synergistic induction of heme oxygenase-1 by the components of the antioxidant supplement Protandim

Kalpana Velmurugan [a,b], Jawed Alam [c], Joe M. McCord [d], Subbiah Pugazhenthi [a,b,*]

[a] Division of Endocrinology, Department of Medicine,
[b] Section of Endocrinology, Veterans Affairs Medical
[c] Department of Molecular Genetics, Ochsner Medica
[d] Division of Pulmonary Sciences, Department of Me

ARTICLE INFO

Article history:
Received 8 July 2008
Revised 23 September 2008
Accepted 31 October 2008
Available online 17 November 2008

Keywords:
Oxidative stress
Heme oxygenase-1
Synergy
Curcumin
Protandim

Available online at www.sciencedirect.com
SCIENCE DIRECT
Free Radical Biology & Medicine 40 (2006) 341 – 347
www.elsevier.com/locate/freeradbiomed

Original Contribution

The induction of human superoxide dismutase and catalase in vivo: A fundamentally new approach to antioxidant therapy

Sally K. Nelson [a,b], Swapan K. Bose [a], Gary K. Grunwald [c], Paul Myhill [d], Joe M. McCord [a,b,d,*]

[a] Webb-Waring Institute for Cancer, Aging and Antioxidant Research, University of Colorado Denver Health Sciences Center, Denver, CO 80262, USA
[b] Department of Medicine, University of Colorado Denver Health Sciences Center, Denver, CO 80262, USA
[c] Department of Preventive Medicine and Biometrics, University of Colorado Denver Health Sciences Center, Denver, CO 80262, USA
[d] Lifeline Therapeutics, Denver, CO, USA

Received 22 June 2005; revised 24 August 2005; accepted 28 August 2005

Abstract

A composition consisting of extracts of five widely studied medicinal plants (Protandim) was administered to healthy human subjects ranging in age from 20 to 78 years. Individual ingredients were selected on the basis of published findings of induction of superoxide dismutase (SOD) and/or catalase in rodents in vivo, combined with evidence of decreasing lipid peroxidation. Each ingredient was present at a dosage sufficiently low to avoid any accompanying unwanted pharmacological effects. Blood was analyzed before supplementation and after 30 and 120 days of supplementation (675 mg/day). Erythrocytes were assayed for SOD and catalase, and plasma was assayed for lipid peroxidation products as thiobarbituric acid-reacting substances (TBARS), as well as uric acid, C-reactive protein, and cholesterol (total, LDL, and HDL). Before

Contents lists available at SciVerse ScienceDirect
Molecular Aspects of Medicine
journal homepage: www.elsevier.com/locate/mam

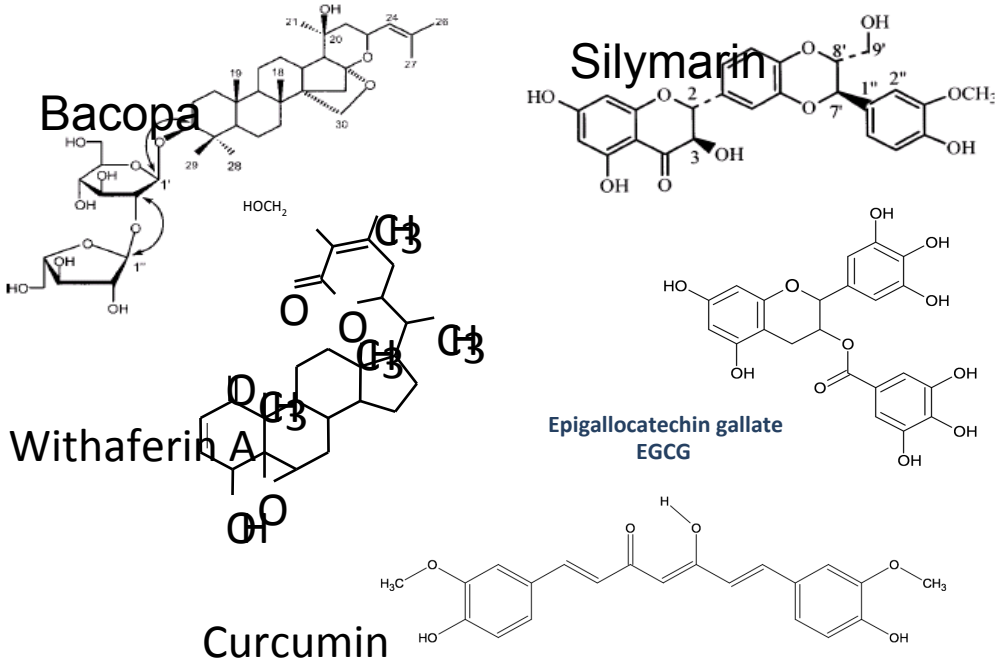
Oxidative Stress in Health and Disease: The Therapeutic Potential of Nrf2 Activation

Brooks M. Hybertson,[a,b] Bifeng Gao,[a] Swapan K. Bose[a] and Joe M. McCord[a,b]

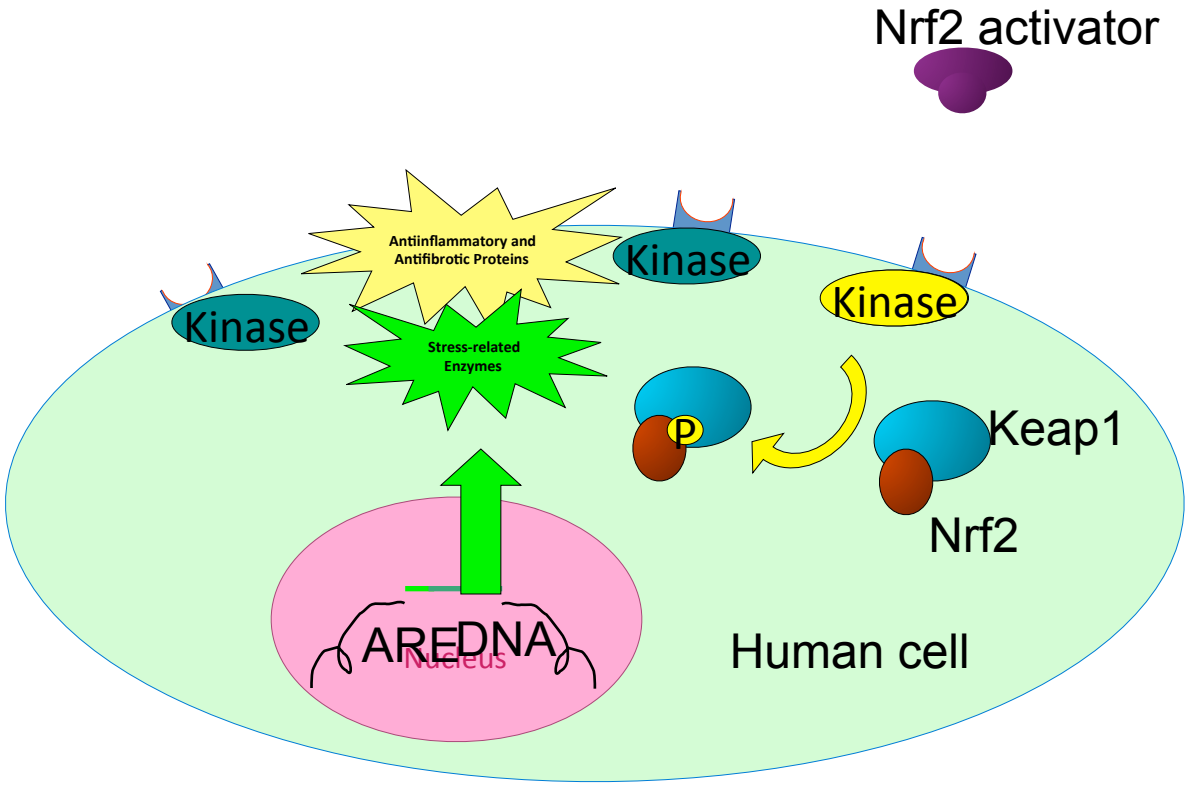
[a]Department of Medicine, Division of Pulmonary Science and Critical Care Medicine, University of Colorado at Denver, Aurora, CO 80045
[b]LifeVantage Corporation, 10813 S. Riverfront Parkway, South Jordan, UT 84095

LifeVantage

Nrf2 = a powerful "master regulator" of antioxidant enzymes and survival genes



LifeVantage



LifeVantage

Available online at www.sciencedirect.com
SCIENCE DIRECT
Free Radical Biology & Medicine 40 (2006) 341 – 347
www.elsevier.com/locate/freeradbiomed

Original Contribution

The induction of human superoxide dismutase and catalase in vivo: A fundamentally new approach to antioxidant therapy

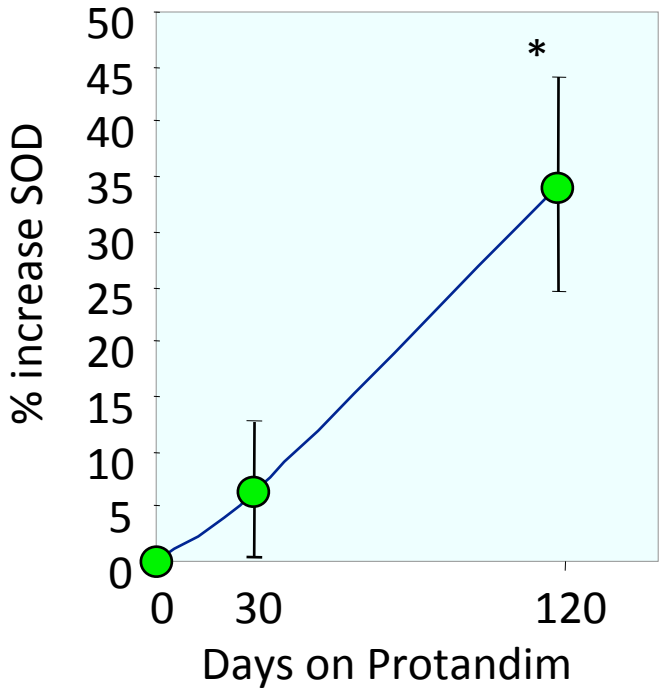
Sally K. Nelson [a,b], Swapan K. Bose [a], Gary K. Grunwald [c], Paul Myhill [d], Joe M. McCord [a,b,d,*]

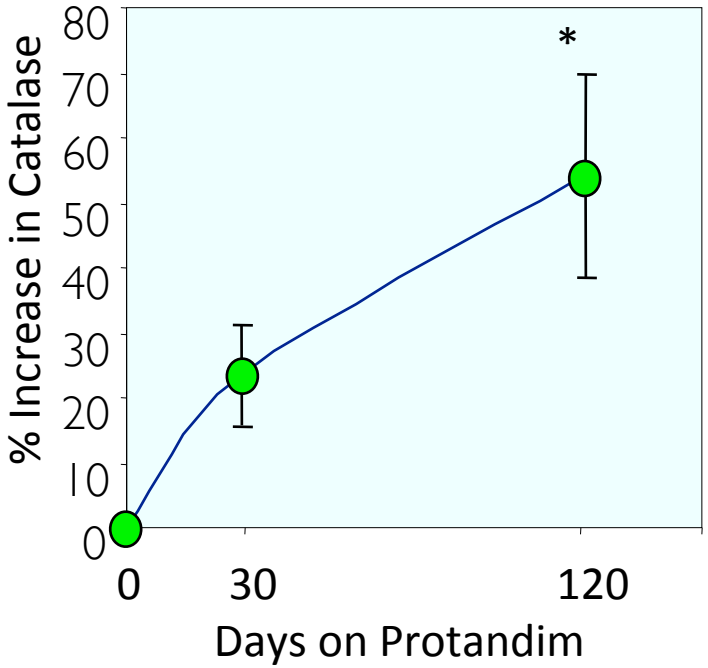
[a] *Webb-Waring Institute for Cancer, Aging and Antioxidant Research, University of Colorado Denver Health Sciences Center, Denver, CO 80262, USA*
[b] *Department of Medicine, University of Colorado Denver Health Sciences Center, Denver, CO 80262, USA*
[c] *Department of Preventive Medicine and Biometrics, University of Colorado Denver Health Sciences Center, Denver, CO 80262, USA*
[d] *Lifeline Therapeutics, Denver, CO, USA*

Received 22 June 2005; revised 24 August 2005; accepted 28 August 2005

Abstract

A composition consisting of extracts of five widely studied medicinal plants (Protandim) was administered to healthy human subjects ranging in age from 20 to 78 years. Individual ingredients were selected on the basis of published findings of induction of superoxide dismutase (SOD) and/or catalase in rodents in vivo, combined with evidence of decreasing lipid peroxidation. Each ingredient was present at a dosage sufficiently low to avoid any accompanying unwanted pharmacological effects. Blood was analyzed before supplementation and after 30 and 120 days of supplementation (675 mg/day). Erythrocytes were assayed for SOD and catalase, and plasma was assayed for lipid peroxidation products as thiobarbituric acid-reacting substances (TBARS), as well as uric acid, C-reactive protein, and cholesterol (total, LDL, and HDL). Before supplementation, TBARS showed a strong age-dependent increase. After 30 days of supplementation, TBARS declined by an average of 40% ($p = 0.0001$) and the age-dependent increase was eliminated. By 120 days, erythrocyte SOD increased by 30% ($p < 0.01$) and catalase by 54% ($p < 0.002$). We conclude that modest induction of the catalytic antioxidants SOD and catalase may be a much more effective approach than supplementation with antioxidants (such as vitamins C and E) that can, at best, stoichiometrically scavenge a very small fraction of total oxidant production.



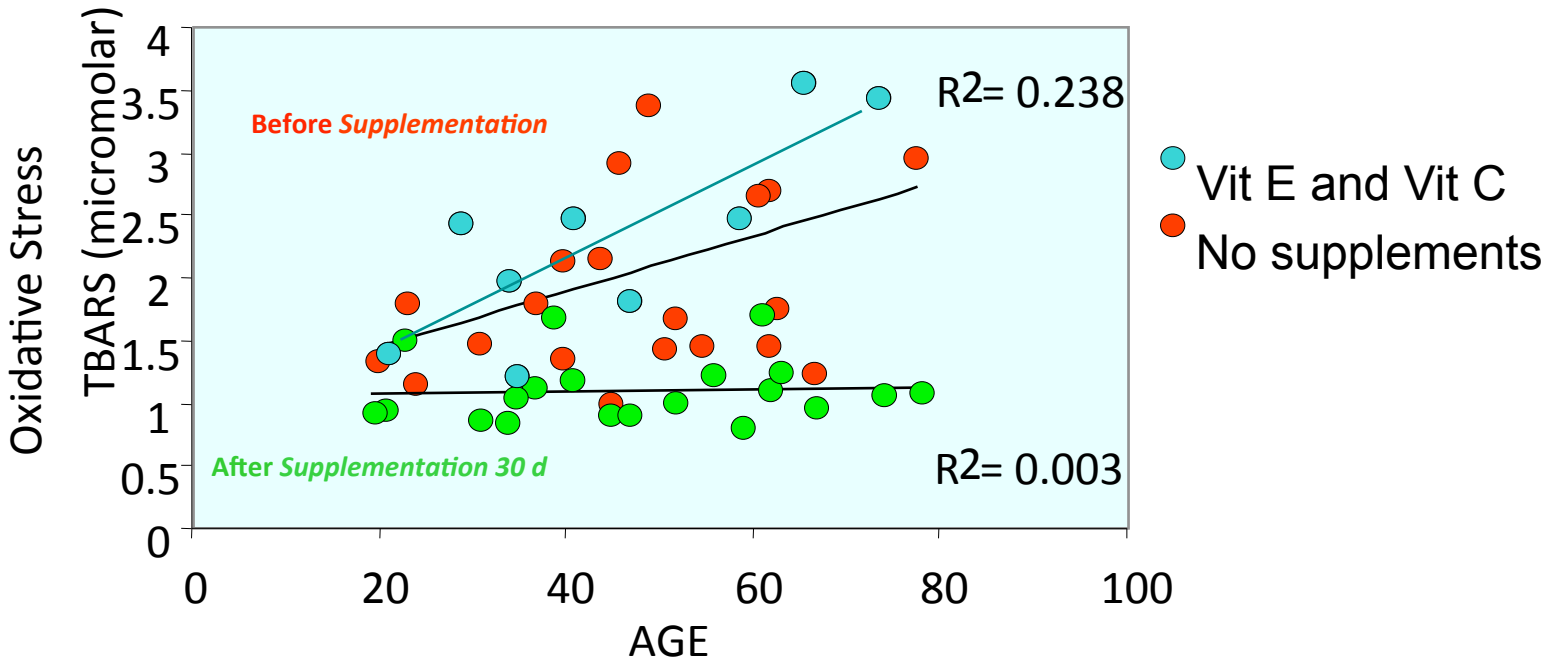


After 120 days…

SOD increased by 34%

Catalase increased by 54%

LifeVantage



After 30 days…

"Remarkably, this age-dependent increase in TBARS was almost completely abolished by ["herbal blend"] treatment (Fig. 1D), with an overall average reduction of the oxidative stress marker by 40%."

LifeVantage

"Healthy-Stressed" Subjects

Screened for "moderate" levels of psychological stress

- Followed for 8-12 weeks…
  - **S**tress Management
  - **E**xercise
  - **N**utrition
  - **S**upplementation
  - **E**valuation

LifeVantage

The Helping Hand

Fruits & Veggies

Lean Protein

Concentrated Carbs

Added Fat

Metabolic Controllers

LifeVantage.

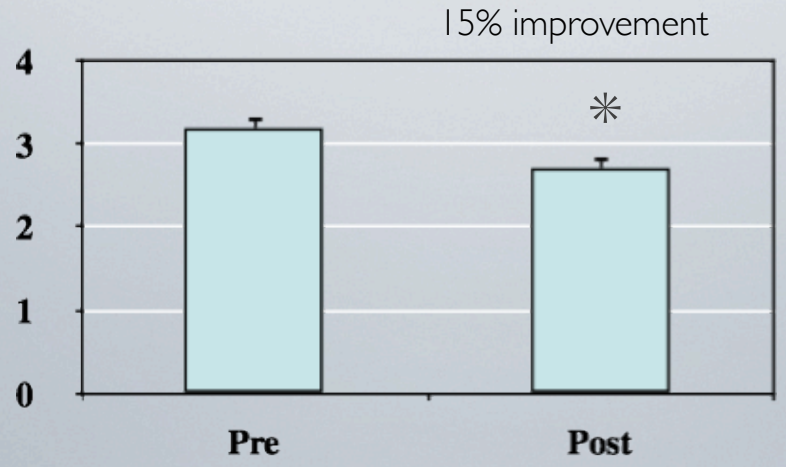
Adaptogenic Supplements

- *Eurycoma longifolia* root extract (Eurypeptides)
- *Citrus sinensis* peel extract (PMFs)
- *Camellia sinensis* leaf extract (Catechins)
- L-Theanine (pure amino acid)
- *Cordyceps sinensis* mycelia extract (Cordycepic acid)
- *Rhodiola rosea* root extract (Rosavin)
- *Eleuthercoccus senticoccus* root extract (Eleutherosides)
- *Withania somnifera* root extract (Withanolides)
- *Magnolia officinalis* root extract (Honokiol)

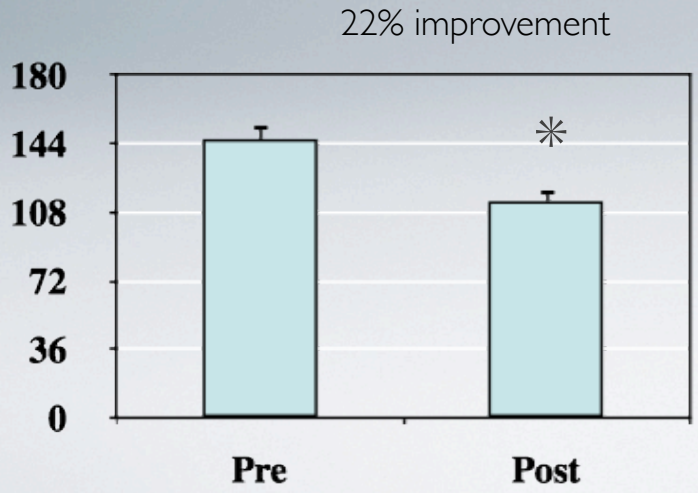
- Intended to:
  - Maintain "Metabolic Balance"
    - Cortisol:Testosterone, Dopamine:Norepinephrine, Serotonin, etc…
  - Deliver Healthy Energy (VIGOR)
  - Enhance Mood

LifeVantage

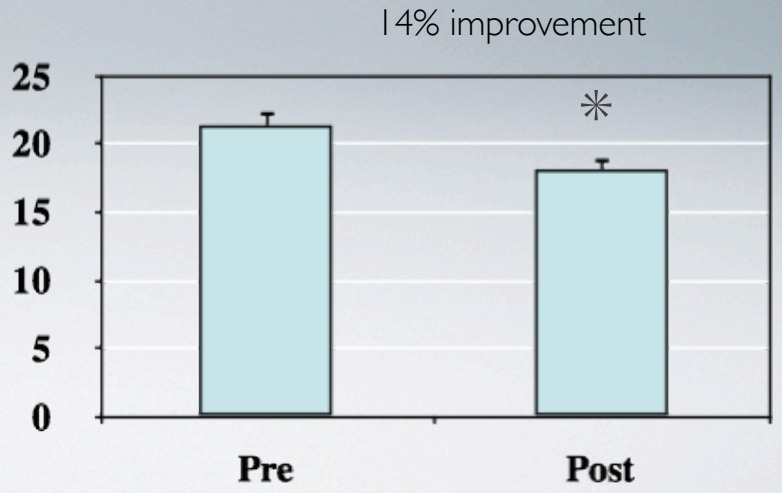
C:T Ratio (x1000)



Global Mood State (POMS)



Subjective Stress



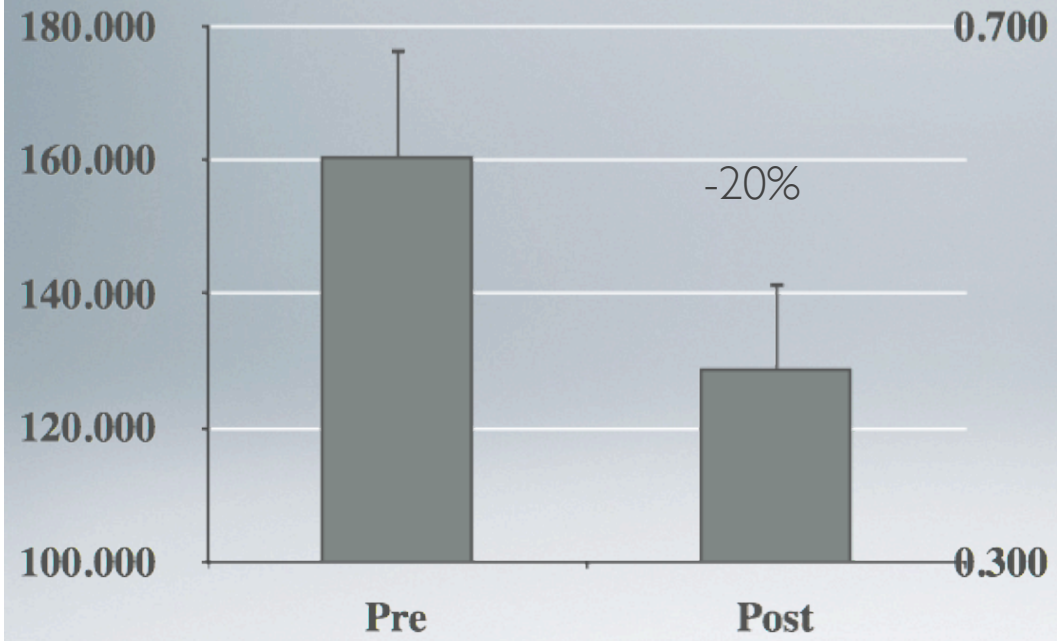
All, $p \leq 0.05$ compared to pre value

LifeVantage

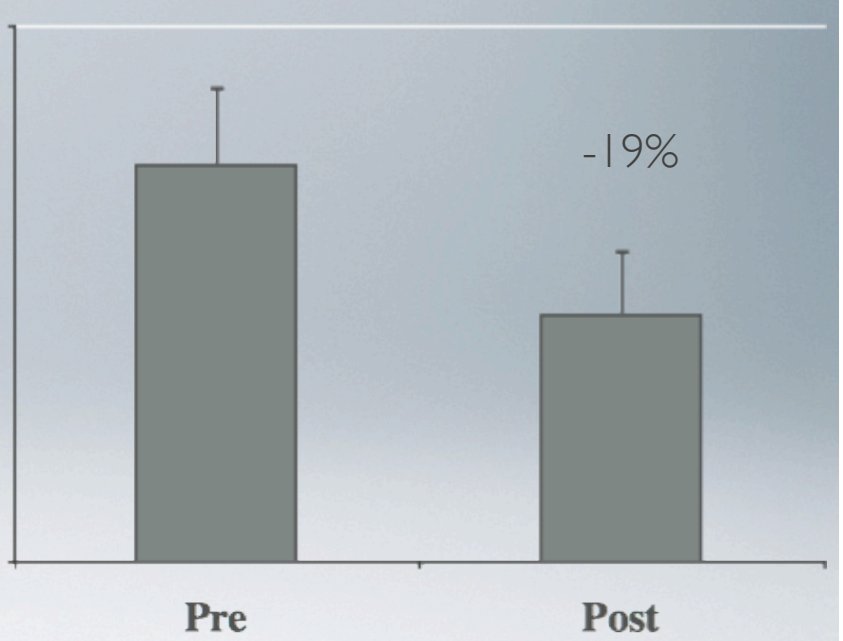
RESULTS

Global Mood State & Salivary Cortisol

Global Mood State (POMS)



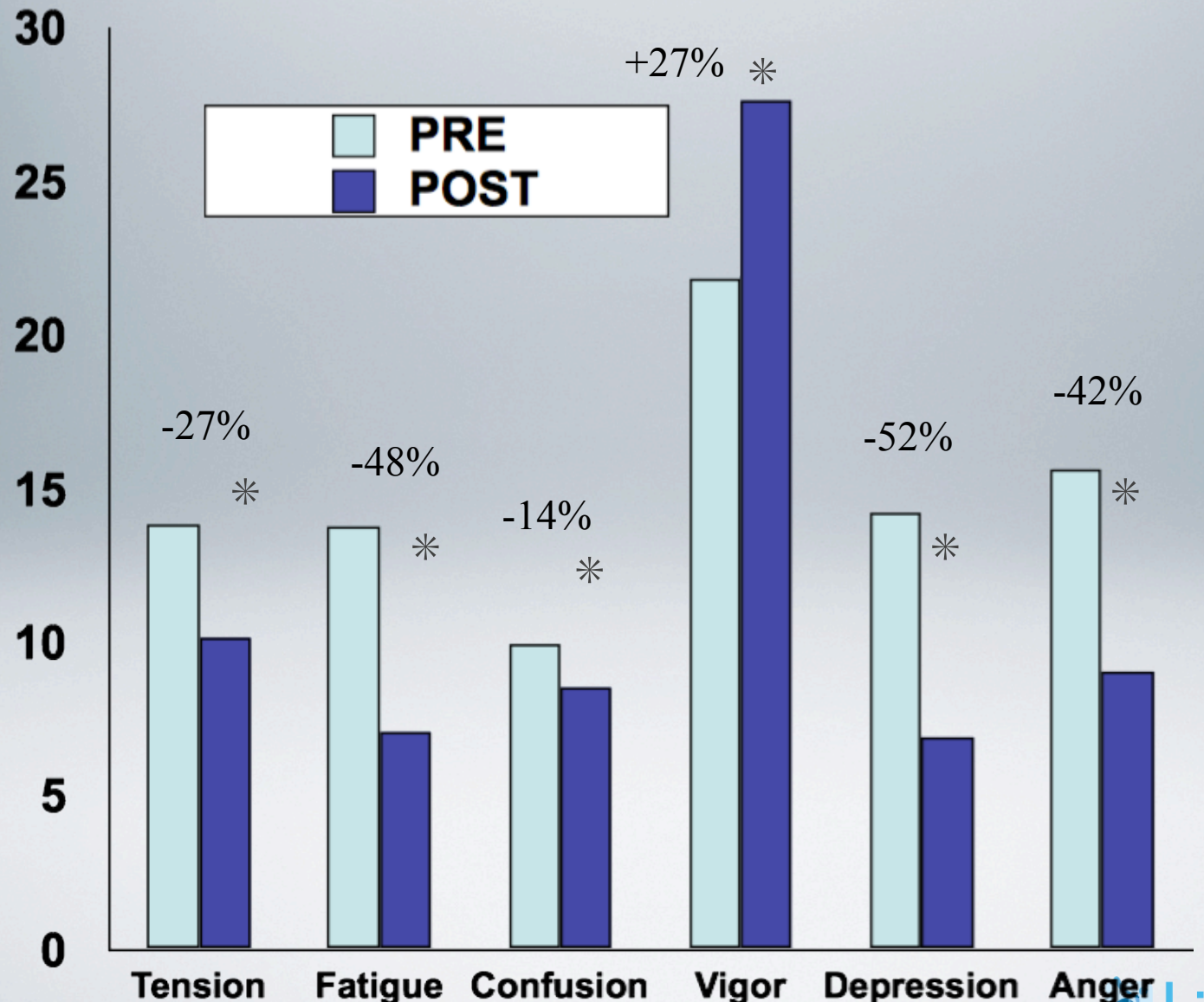
Salivary Cortisol (ug/dL)



Both, $p \leq 0.05$ compared to pre value

LifeVantage

Profile of Mood States (POMS)



All, $p \leq 0.05$ compared to pre value

LifeVantage.

Dietary Supplement Combination Reduces Inflammation and Improves Mood State in Stressed Subjects

S. Talbott[1], J. Talbott[1], M. Vosti[2], & J. Anderson[2]

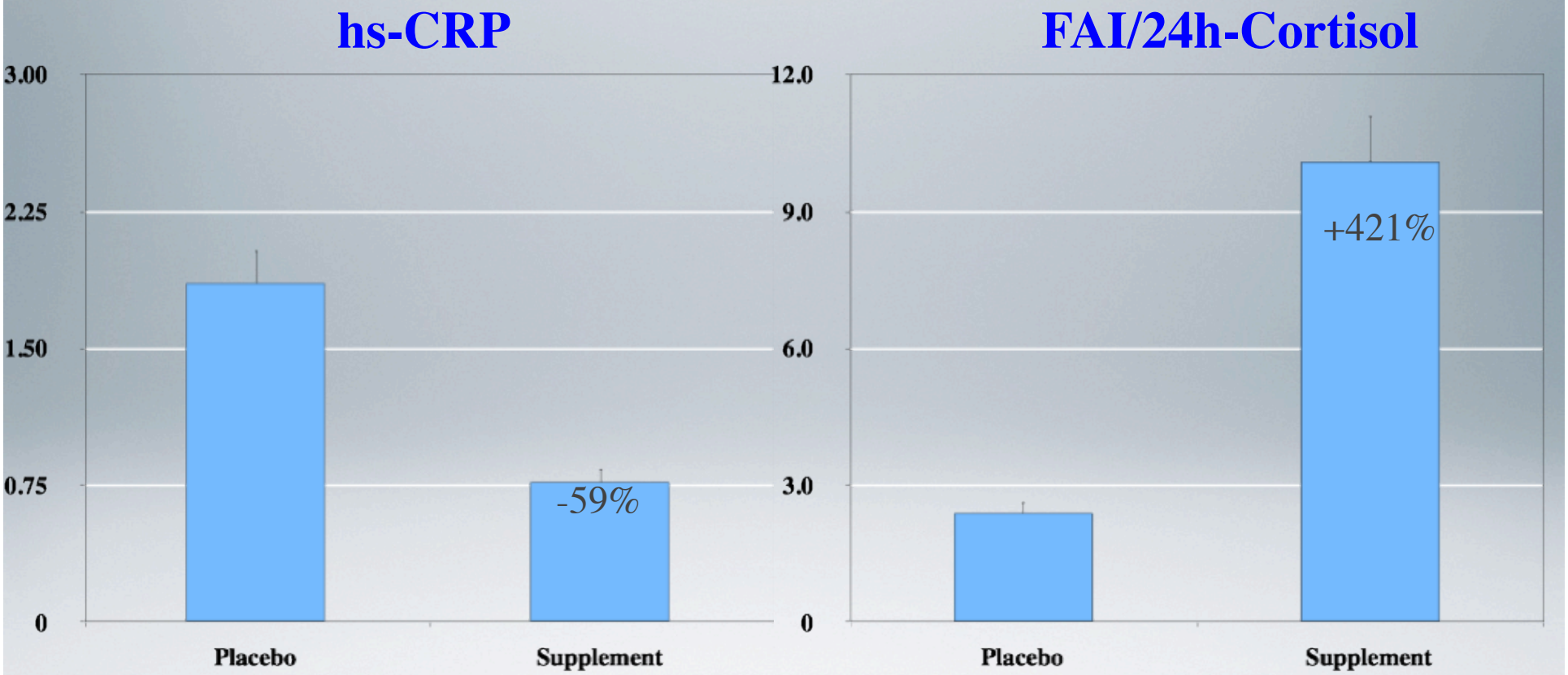
[1]SupplementWatch & [2]South Mountain Chiropractic, Salt Lake City (Draper), UT

SUPPLEMENT WATCH
Supplement Decisions Made Easy

LifeVantage.

RESULTS (week 4)

Inflammation & Metabolic Balance



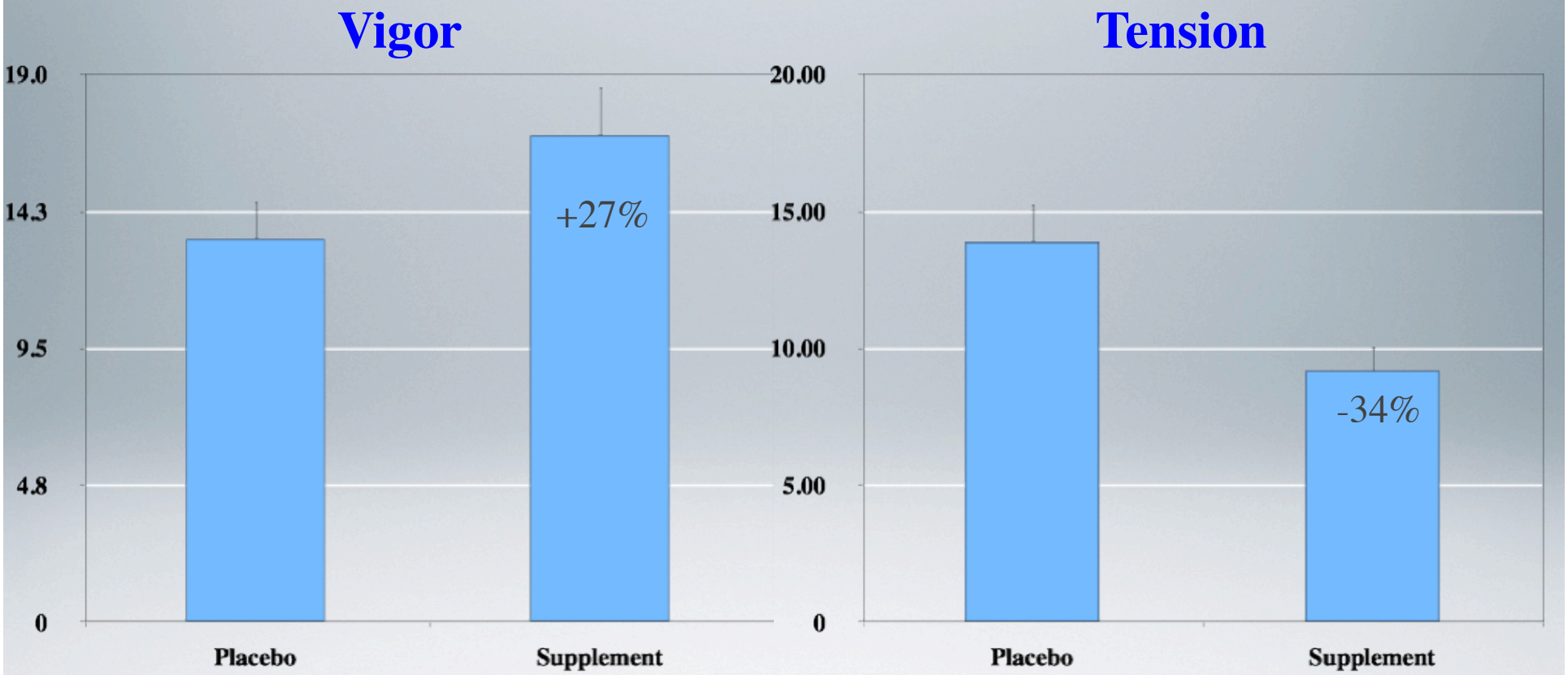
Both, $p \leq 0.05$ compared to Placebo

SUPPLEMENT WATCH
Supplement Decisions Made Easy

LifeVantage

RESULTS (week 4)

Profile of Mood States (POMS)



Both, $p \leq 0.05$ compared to Placebo

SUPPLEMENT WATCH
Supplement Decisions Made Easy

LifeVantage

Effect of *Eurycoma longifolia* Extract on Anabolic Balance During Endurance Exercise

S. Talbott, J. Talbott, J. Negrete, M. Nichols, and J. Roza

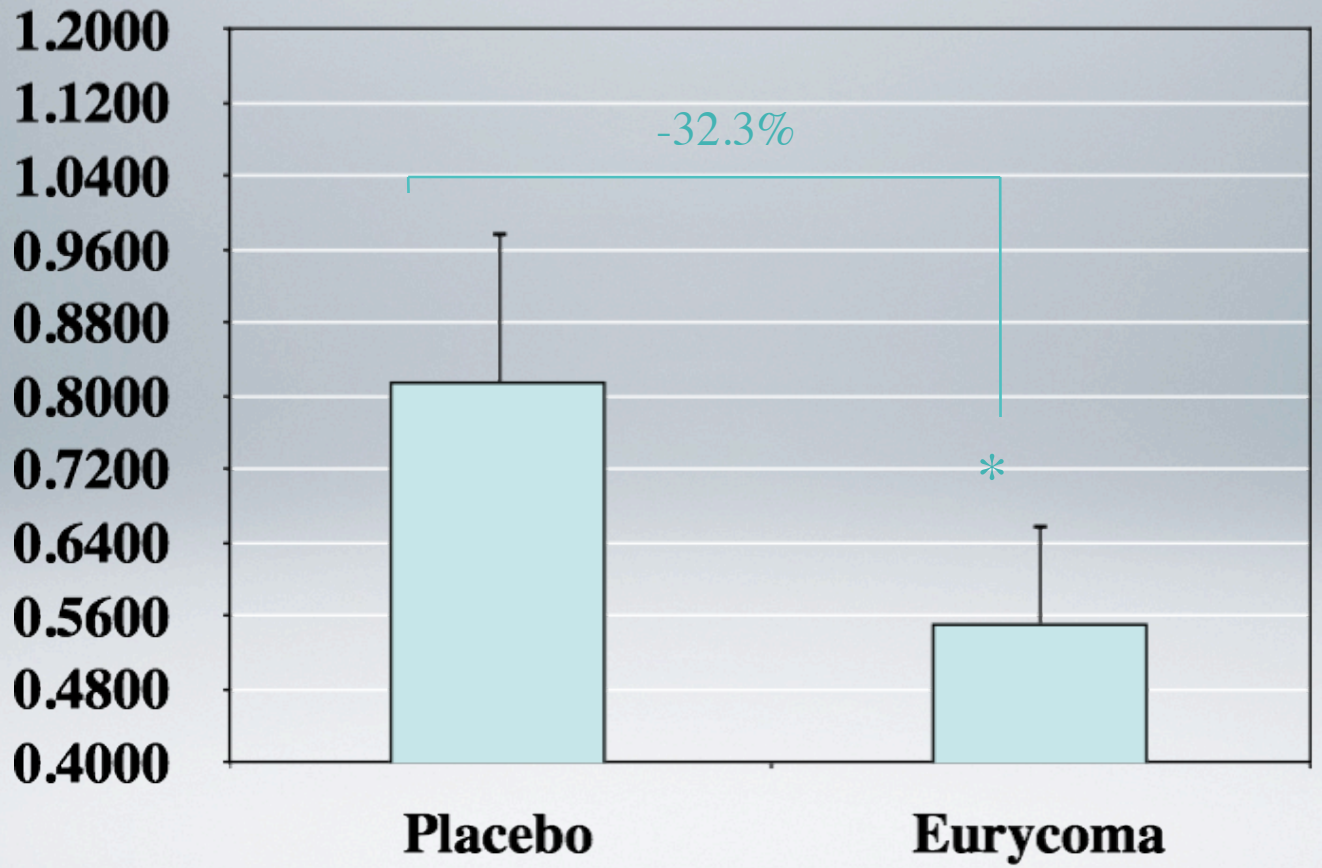
SupplementWatch, Inc., Salt Lake City (Draper), UT

& Source One Global, Chicago, IL

LifeVantage.

RESULTS

Salivary Cortisol (ug/dL)



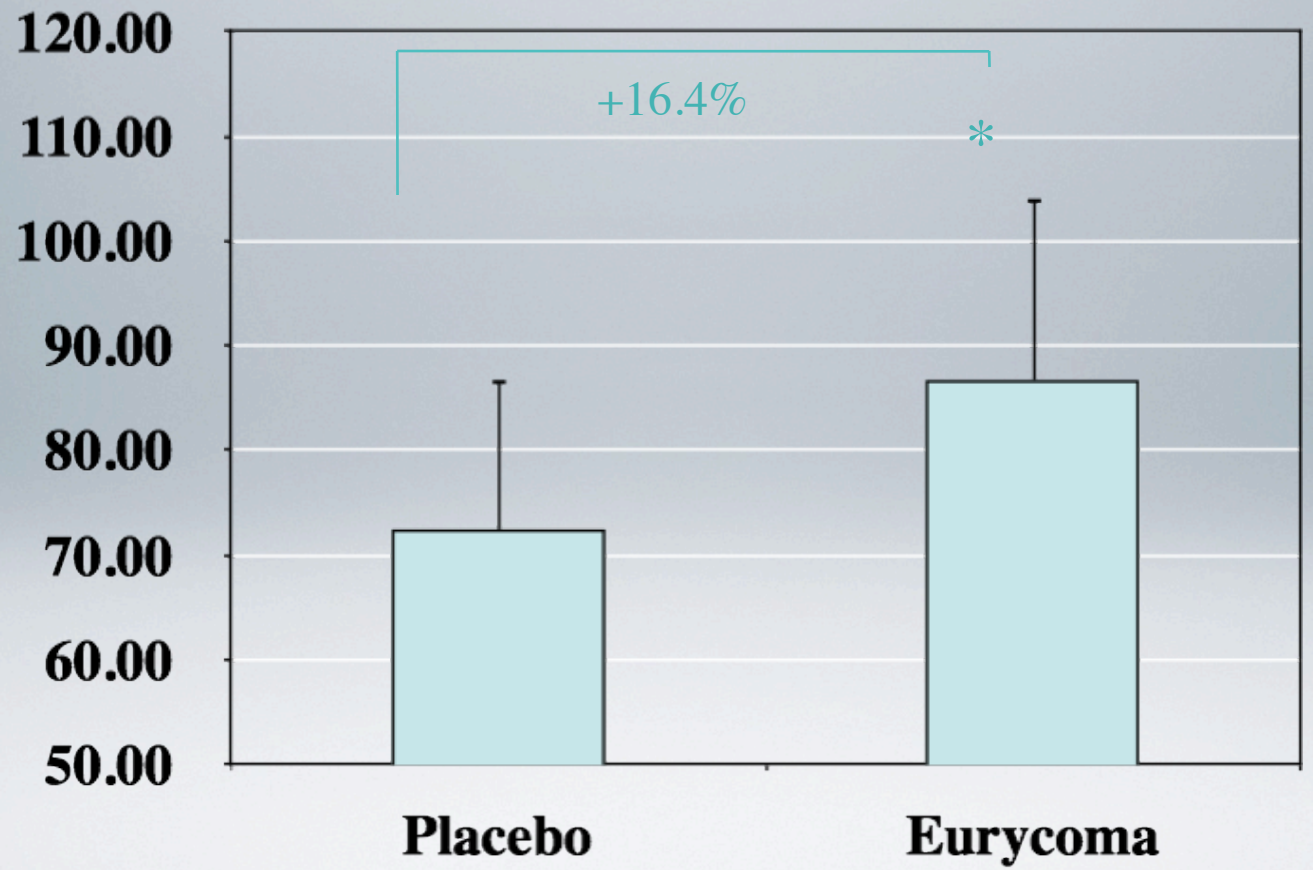
*p ≤ 0.05 compared to Placebo

SUPPLEMENT WATCH
Supplement Decisions Made Easy

LifeVantage

RESULTS

Salivary Testosterone (pg/dL)



*p ≤ 0.05 compared to Placebo

SUPPLEMENT WATCH
Supplement Decisions Made Easy

LifeVantage

Effect of Branched Chain Amino Acids on Salivary Cortisol Levels During Endurance Exercise

S. Talbott, J. Talbott, J. Negrete, and M. Nichols

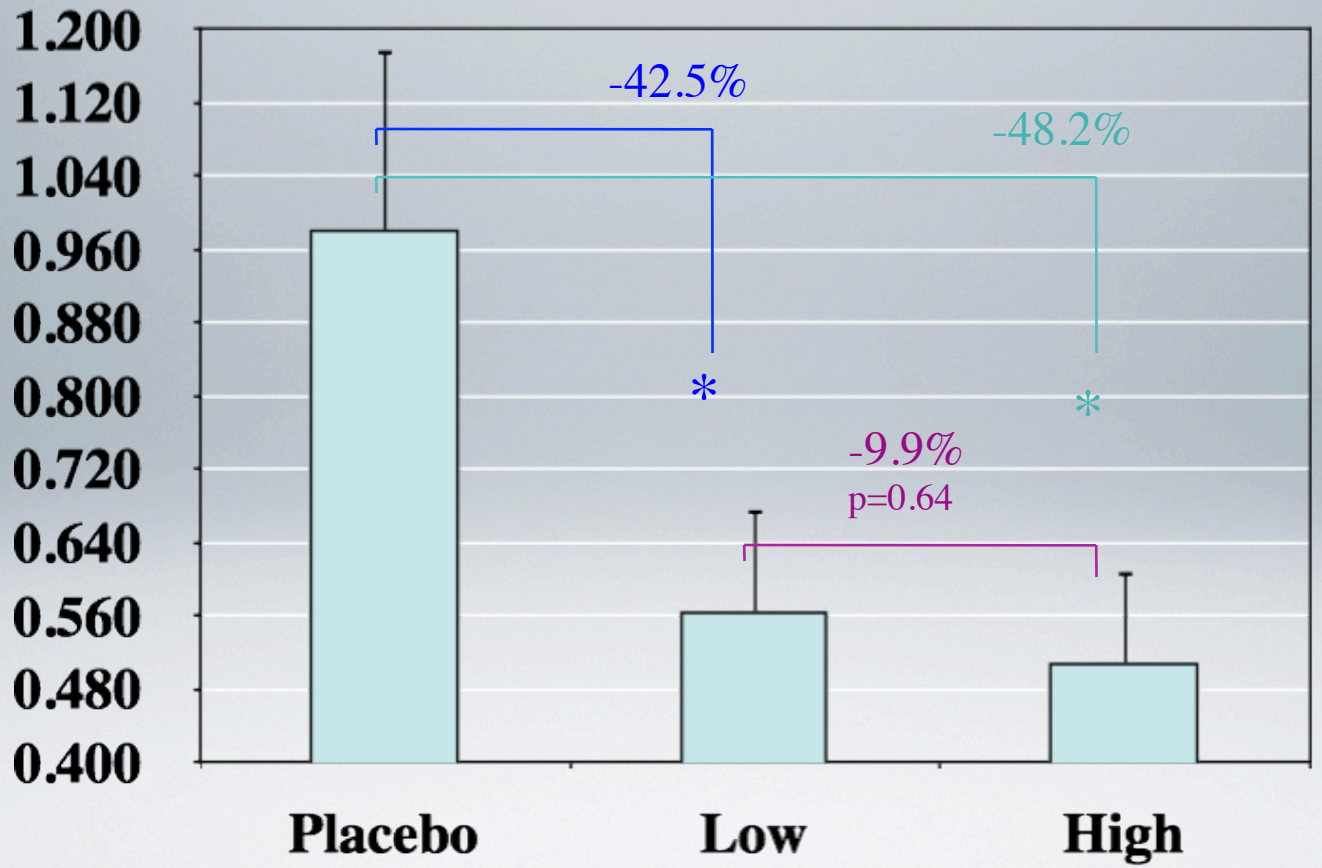
SupplementWatch, Inc.

Salt Lake City (Draper), UT

LifeVantage

RESULTS

Salivary Cortisol (ug/dL)



*p ≤ 0.05 compared to Placebo

SUPPLEMENT WATCH
Supplement Decisions Made Easy

LifeVantage

Effect of *Eurycoma longifolia* and *Magnolia officinalis* on Hormone Balance & Mood State in Stressed Subjects

S. Talbott[1,2], J. Talbott[1], & M. Pugh[2]

[1]SupplementWatch & [2]MonaVie, Salt Lake City, UT

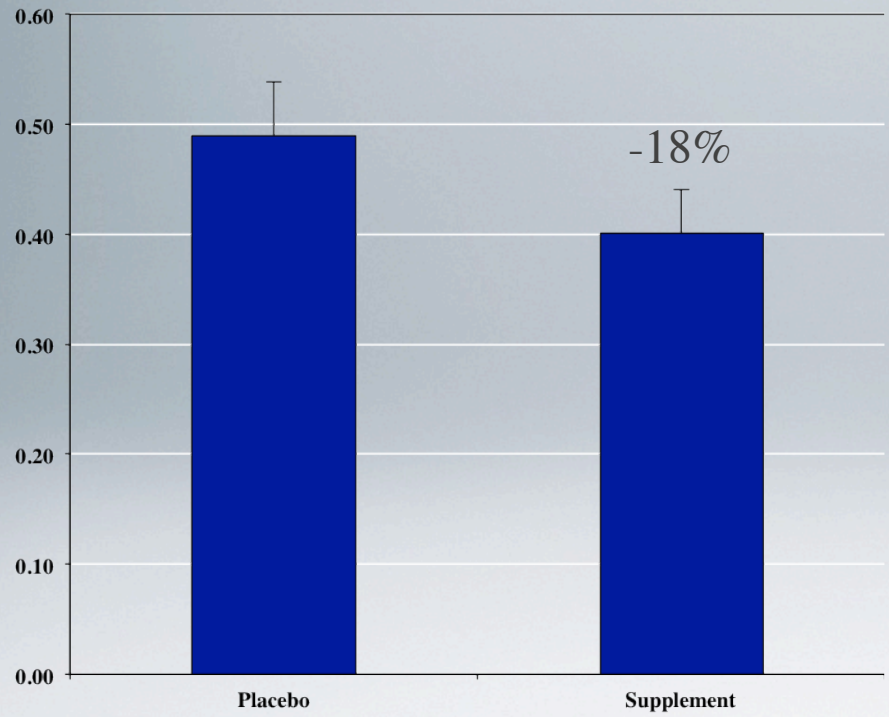
SUPPLEMENT WATCH
Supplement Decisions Made Easy

LifeVantage

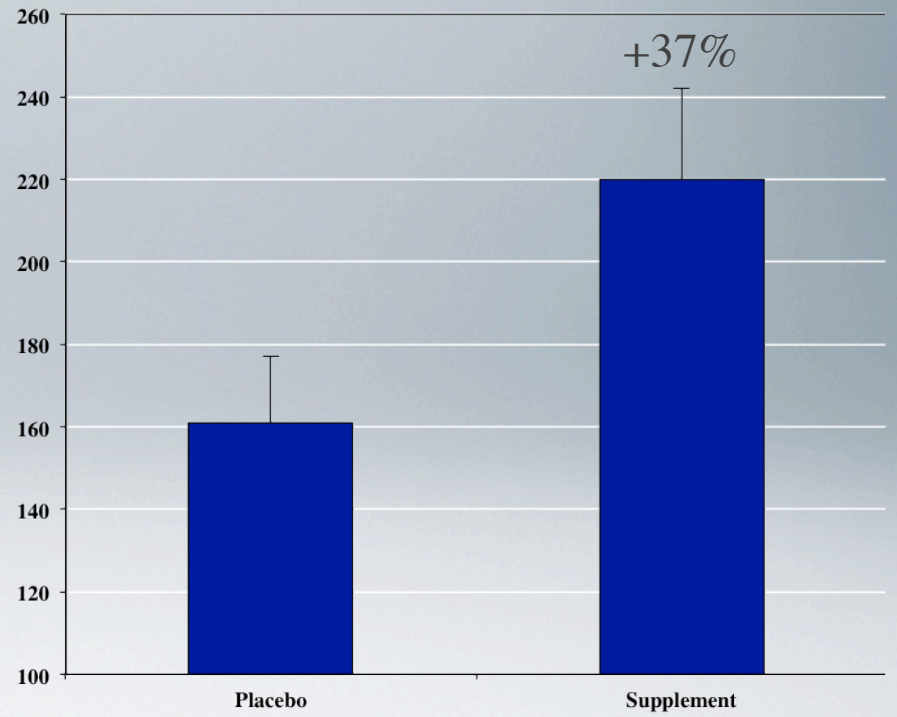
RESULTS (week 4)

Cortisol & Testosterone (% difference from Placebo)

Cortisol, ug/mL (Magnolia)



Testosterone, pg/mL (Eurycoma)



Both, $p \leq 0.05$ compared to Placebo

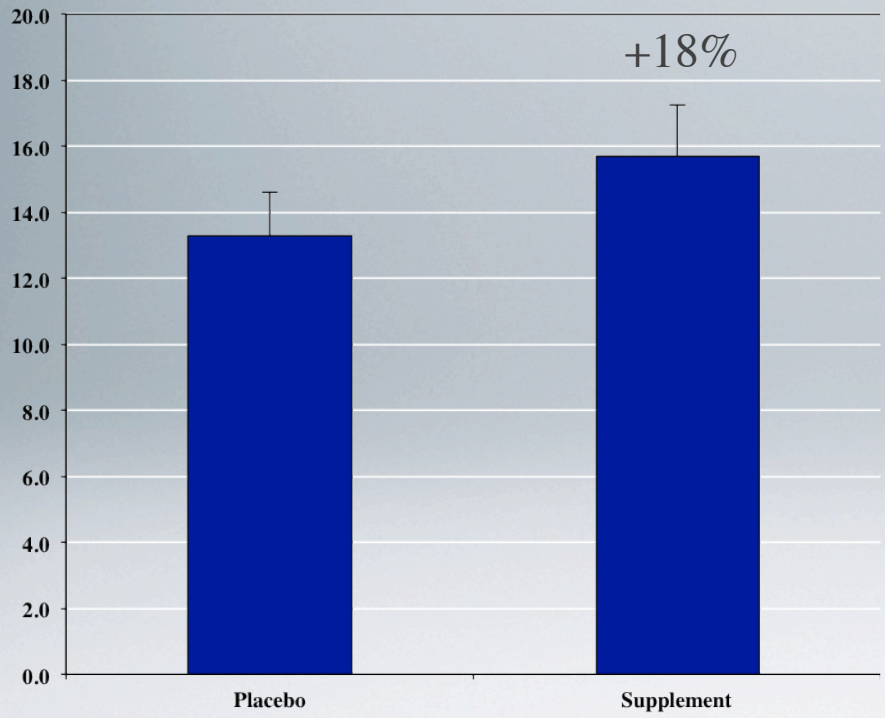
SUPPLEMENT WATCH
Supplement Decisions Made Easy

LifeVantage

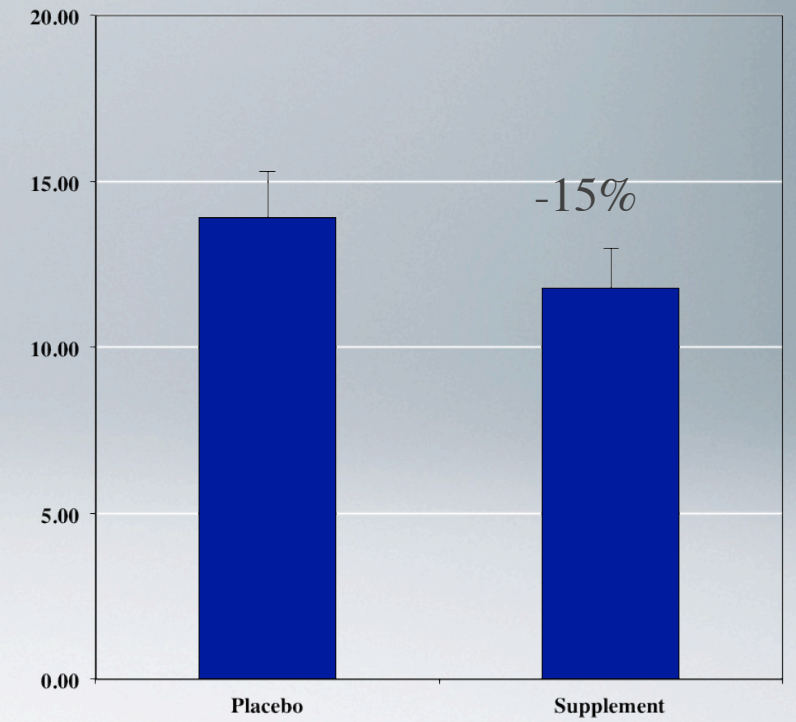
RESULTS (week 4)

Profile of Mood States (POMS)

Vigor (Magnolia)



Tension (Eurycoma)



Both, $p \leq 0.05$ compared to Placebo

SUPPLEMENT WATCH
Supplement Decisions Made Easy

LifeVantage

Conclusions

- Top reasons for primary care visits involve Stress, Fatigue, Depression
- There is a strong scientific association between chronic metabolic imbalance & stress-related diseases (stress, oxidation, inflammation).
- Effect **magnitude** (~20% Global Mood & Vigor) is equivalent to:
  - Pharmaceutical treatment (Prozac, Zoloft, Celexa, etc)
  - CBSM (cognitive behavioral stress management)
- Restoring "Biochemical Balance" can:
  - enhance weight loss
    - metabolic effect
  - improve dietary compliance
    - behavioral effect
  - enhance mood state & vigor
    - psychological effect

LifeVantage