

Anti-Aging Medications What is the Evidence?

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Outline

- Introduction
- Oxidative damage
- Antioxidants properties
- Antioxidants and antiaging interventions
- Hormonal therapy
- Benefits of DHEA, testosterone, and GH in longevity
- Conclusion

Introduction

- Interest is rising
- Baby-boomer generation
- Progress is being made in understanding aging
- Public has more access to information resources



Oxidative Damage

- Free radical oxidative damage
- Biological organisms develop defense mechanism
- A balance must be maintained between free radical formation and antioxidant production
- The human organism cannot synthesize carotenoids and vitamins as opposed to

Anti-Aging Interventions

- Modifications of the biochemical and molecular events
- Correct the physiological changes
- Decrease the susceptibility to disease associated with aging

Anti-Aging Interventions

- Restore your hormone to young adult level
- Avoid:
 - Age related illnesses
 - Reverse your biological age
 - Extend your life expectancy
 - Improve your quality of the additional years

Cerebrovascular and Cardiovascular Effect

Physicians' Health Study

(Analysis of a prospective cohort study)

83,629 US male physicians



29% took Vitamin E, C or Multi



No decrease in total cardiovascular disease or
CHD mortality

Physicians' Health Study

43,738 men 40 to 75 years old: no
cardiovascular disease or diabetes



Vitamin E, C & Carotenoid



No reduction in risk of stroke

The Heart Outcome Prevention Evaluation (HOPE) Trial

Patients 55 years or older: cardiovascular disease or diabetes



Vitamin E 400 IU daily: average 4.5 years



No effect on cardiovascular outcomes

Alpha-Tocopherol, Beta Carotene Cancer Prevention Study

26,593 male smokers 50 to 69 years old



Beta-carotene intake (20 mg)



Decrease risk of stroke (RR 0.47)

Antioxidants and Lipids

120 subject age 50 & older: no
cardiovascular disease



Vitamin C (1g) & E (100IU) alone or in
combination



Decrease TC, LDL & Increase HDL

Antioxidants and Lipids

160 patients < 70 years: coronary heart disease



Vitamin E 800 IU , C 1 gm , Beta-Carotene 25 mg & Selenium 100 mcg



Improve the benefits of simvastatin & niacin on lipid levels

Antioxidants and Cognition

2,166 elderly people



1st regimen (Vitamin E, C & Beta-Carotene)

2nd regimen (Zinc & Copper)

3rd regimen (1st + 2nd)

4th regimen (Placebo)



With respect to cognition: none was beneficial or harmful ($p > 0.05$)

Antioxidants and Mortality

7 randomized trials of Vitamin E (50 - 800 IU)



No reduction of mortality compared to control

No significant decrease in cardiovascular &
cerebrovascular accident

Antioxidants and Mortality

8 trials of Beta-Carotene (15 to 50 mg)



Small but significant increase in all-cause mortality & cardiovascular death

Antioxidants and Mortality

Meta-analysis: 19 clinical trials



135,967 patients Vitamin E doses
(16.5 to 2,000 IU/day)



11 trials used high dose Vitamin E



Rate of all-cause mortality slightly greater with
Vitamin E than with placebo

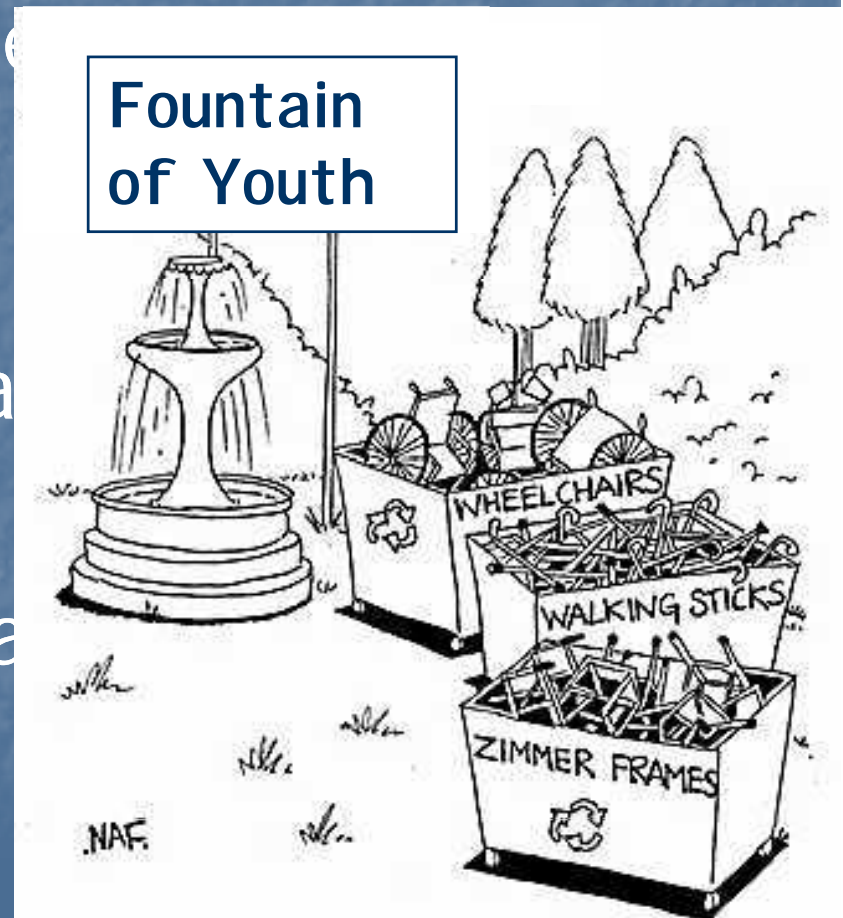
8 trials of low dose Vitamin E: no increase risk of
mortality

Role of Antioxidants as Antiaging

Carotenoids	Vitamin C	Vitamin E
↑ in cardiovascular mortality	Inconsistent data on the lipid profile	No ↓ in risk of stroke & cardiovascular mortality
Inconsistent data on the risk of stroke	No ↓ in cardiovascular mortality	Inconsistent data on lipids, cognition & mortality
↑ in all-cause mortality	No ↓ in the risk of stroke	Insufficient evidence in the treatment of Alzheimer disease

Hormonal Therapy

- Treatment with hormone therapy restores youth
- Hormonal levels: decreased
- Hormones: supplemental replacement



Testosterone

- Testosterone therapy: treatment of hypogonadal men
- Level of testosterone: decline with age
100 ng/dL per decade

Effects of Testosterone

Randomized control study: lasting 1-3 years



Men > 65 years old, with low serum testosterone



Decrease in fat mass, increase in lean mass & BMD
in testosterone treated groups

Testosterone patch: 6 mg/day

- **No improvement in measures of muscle strength, physical performance, energy & sexual function.**

Snyder et al. N Engl J Med 2006;355:1647.

Dehydroepiandrosterone (DHEA)

- Metabolic intermediate
- Levels of DHEA: decrease at a rate of 2%/year



Dehydroepiandrosterone (DHEA)

- **Valenti G. et al:** (Med Sci 2004; 59:466)
Little evidence to suggest DHEA to prolong life or prevent disease
- **Villareal DT et al.:** (JAMA 2004; 292:2243)
Increase in muscle mass & decrease in fat mass with DHEA 50 mg/day
- **Flynn MA et al.:** (J Clin End Met 1999; 84:1527)
No increase in muscle mass & no decrease in fat mass with DHEA 100 mg/day

Dehydroepiandrosterone (DHEA)

- **Nasman B et al.:** (Biol Psychiatry 1991;30:684)
Cognitive dysfunction: associated with low, normal and high DHEA level
- **Vallee M et al:** (Brain Res Rev 2001;37:301)
Patients with low level of DHEA: improvement of learning and memory dysfunction after DHEA intake
- **Wolkowitz et al:** (Neurology 2003;60:1071)
Randomized, double blind placebo control with DHEA: No significant cognitive effect after DHEA intake

Growth Hormone (GH)

- GH declines 14% per decade
- Associated decline in insulin like growth factor
- 1990: studies looked promising
- Randomized controlled trial:
 - GH: increase LBM, decrease fat mass
 - GH: No improvement in strength or aerobic conditions
- Side effects of GH:
 - Carpal tunnel syndrome, edema, arthralgia, diabetes

Growth Hormone (GH)

Randomized controlled trial

500 critically ill patients:



Mortality rate: 2x higher with high dose GH

GH: → GH deficiency
→ AIDS wasting

Takala et al. N Eng J Med 1999;341:785.



Hormones: Antiaging Interventions

Testosterone	DHEA	Growth Hormone
↓ in fat mass & ↑ in lean-mass	Inconsistent data on muscle mass, fat mass & strength	↑ in lean body mass; ↓ in fat mass
Mixed data on the effect on cognition	Insufficient evidence for improvement in cognition	↑ in bone mineral density
		↑ in mortality

Take Home Message

- Antiaging therapies are growing
- Antioxidants: little effect on preventing cerebrovascular and cardiovascular disease
- Antioxidants: Inconsistent data on cognition
- Antioxidants: Not enough data to support

Take Home Message

- **Hormones : their level decline with age**

Testosterone replacement therapy



Decreases fat mass, increase lean mass
Increase muscle strength in hypogonadal
testosterone deficient men

Take Home Message

- **DHEA**

Routine replacement in older adults



No meaningful benefit

- **Growth Hormone**

Risk of therapy in people not GH deficient



Outweighs the benefit

Conclusion

- Future: research should explain more the aging process
- Awareness of clinicians:
Antioxidants and hormonal therapies
- Both categories : minimal effect on improving longevity or functional abilities

Questions?

