Antioxidants, Aging, and Exercise: Is there a paradox?

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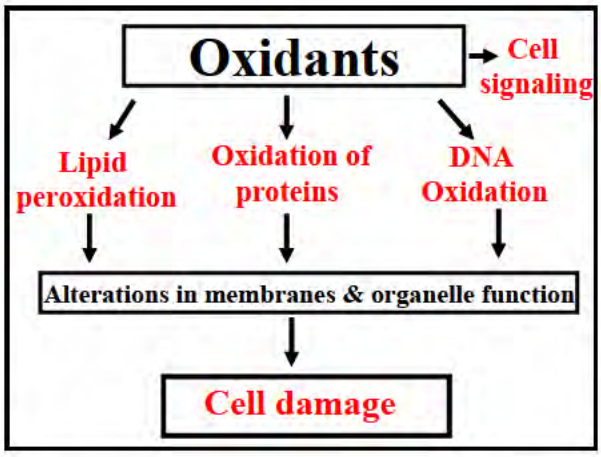
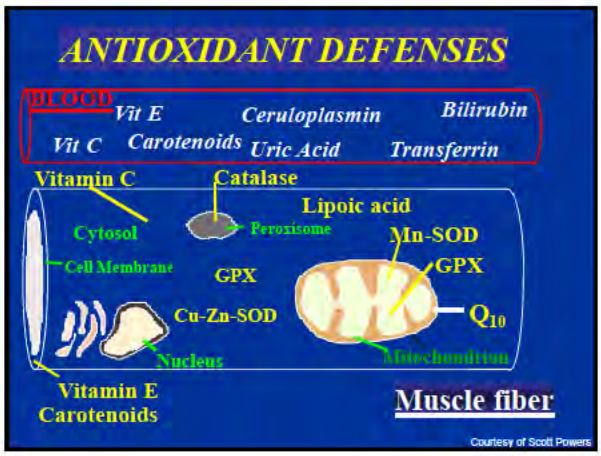
Department of Exercise and Sports Science

What are free radicals and what can they do?

Reduction reaction

Oxidation reaction





Aging is associated with oxidative stress. Should we administer antioxidants to the elderly?

OUTLINE:

- Background
  - oxidative stress and aging
  - aging and exercise
- Free radicals…. from muscle or blood?
- Vascular function, oxidative stress, exercise and antioxidants
- Conclusions

- "twist(s) in the tale"

Oxidative Stress + Aging

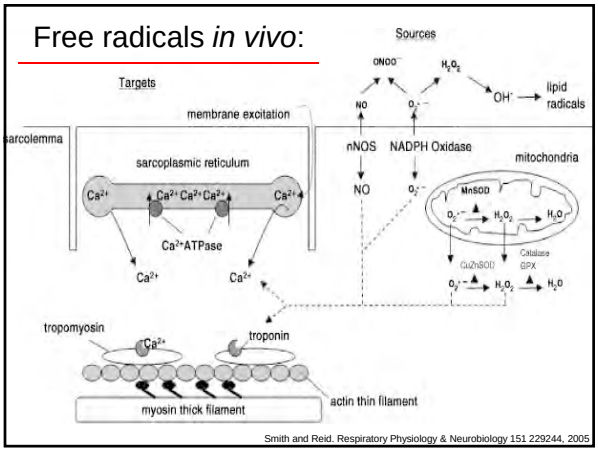
- Denman Harmen 1950's

"Organisms age because cells accumulate free radical damage with the passage of time"

- rate of living theory
- hyperbaric hyperoxia and radiation both damage by free radicals

Rusting – oxidation of metals…..
……. "aging oxidation of humans?"

Free radicals *in vivo*:



Smith and Reid. Respiratory Physiology & Neurobiology 151 229244, 2005

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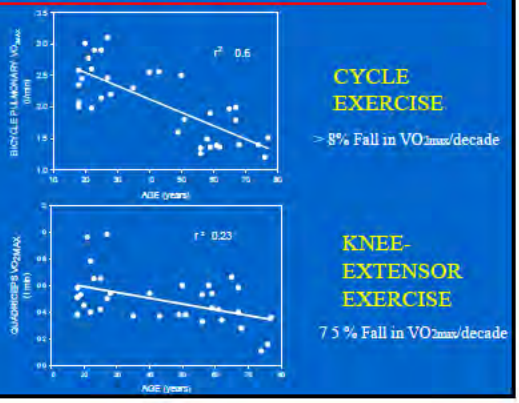
AGE AND EXERCISE CAPACITY



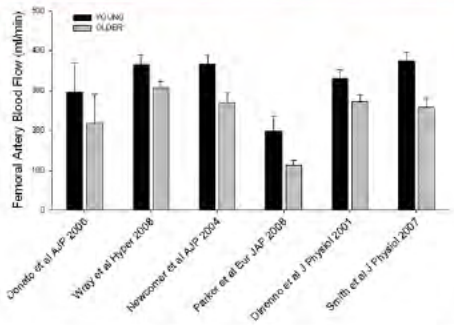
CYCLE EXERCISE

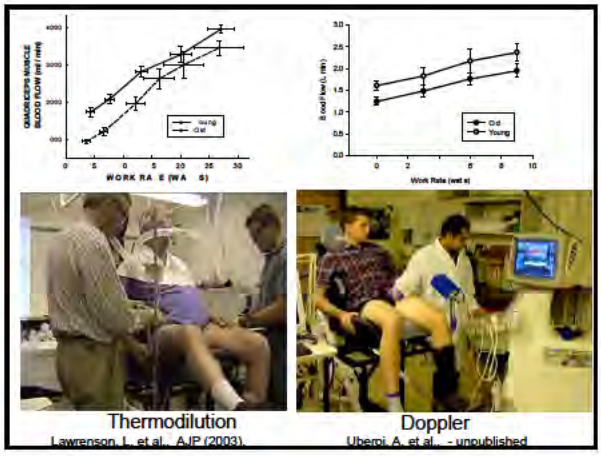
> 8% Fall in VO_{2max}/decade

KNEE-EXTENSOR EXERCISE

7.5 % Fall in VO_{2max}/decade

Attenuated Resting Skeletal Muscle Blood in the Elderly





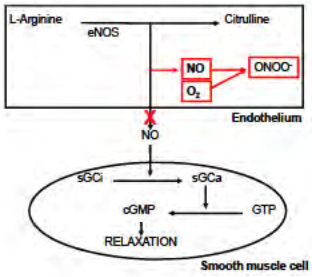
Thermodilution

Lawrenson, L. et al., AJP (2003).

Doppler

Uberoi, A. et al., - unpublished

Endothelium mediated vasodilation and NO bioavailability



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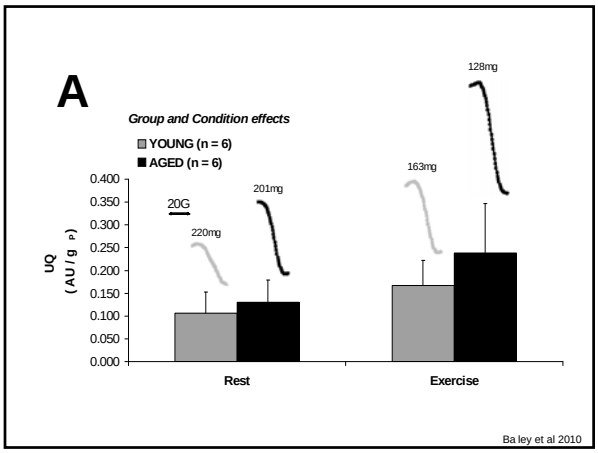
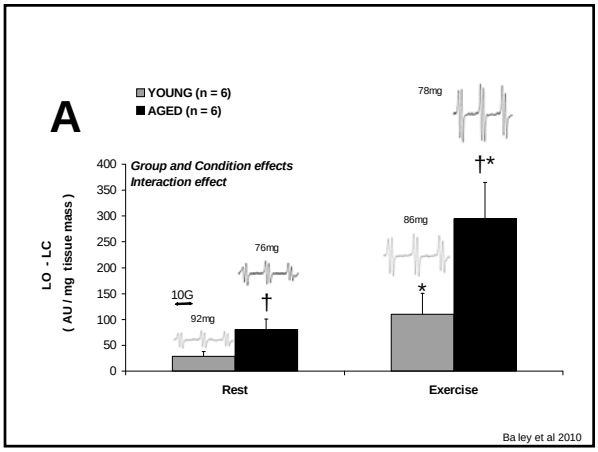
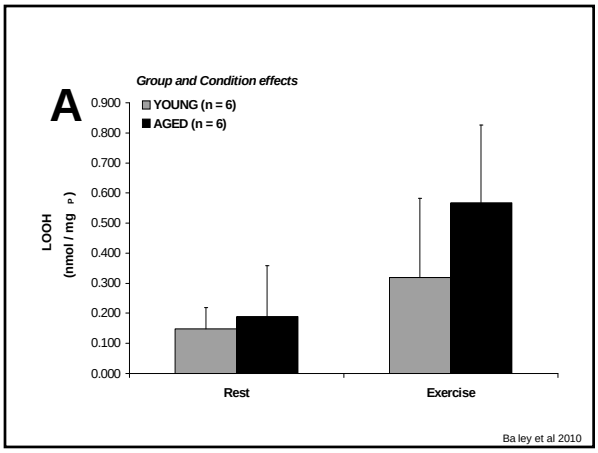
Post-exercise biopsy for low temperature (77K) EPR Spectroscopy

Average end-exercise to sample emersion in liquid N_2 = 20 seconds


A
Group and Condition effects
YOUNG (n = 6)
AGED (n = 6)
UQ
(AU / g P)
0.400
0.350
0.300
0.250
0.200
0.150
0.100
0.050
0.000
20G
220mg
201mg
163mg
128mg
Rest
Exercise
Ba ley et al 2010

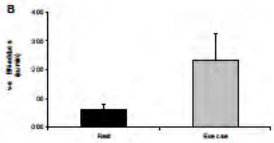

A
YOUNG (n = 6)
AGED (n = 6)
Group and Condition effects
Interaction effect
LO - LC
(AU / mg tissue mass)
400
350
300
250
200
150
100
50
0
10G
92mg
76mg
†
78mg
†*
86mg
*
Rest
Exercise
Ba ley et al 2010


A
Group and Condition effects
YOUNG (n = 6)
AGED (n = 6)
LOOH
(nmol / mg P)
0.900
0.800
0.700
0.600
0.500
0.400
0.300
0.200
0.100
0.000
Rest
Exercise
Ba ley et al 2010

EPR Spin-trapping across an exercising muscle

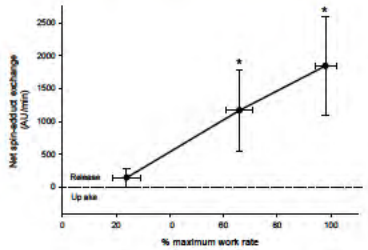
α-phenyl-*tert*-butylnitrone (PBN)-adducts

-Carbon centered alkyl radicals
-Oxygen centered alkoxyl radicals



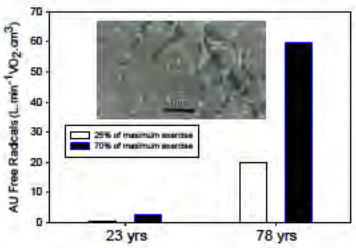
Bailey et al. J. App. Physiol. 2003

Free radical outflow from an exercising muscle with increasing work



Bailey et al. J. App. Physiol. 2003

Age-related difference in free radical outflow from exercising muscle



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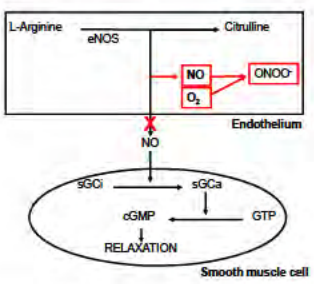
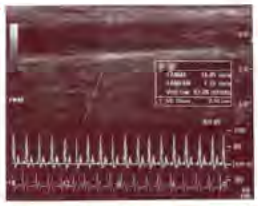
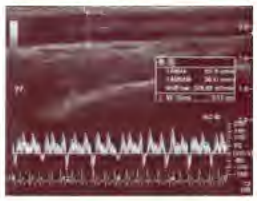


Doppler ultrasonography:

Rest

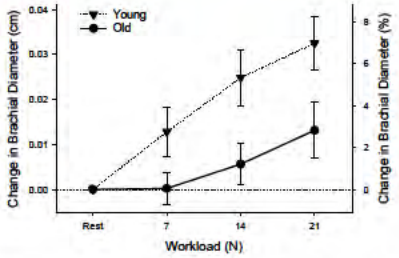


Exercise



Donato *et al.* AJP 2010

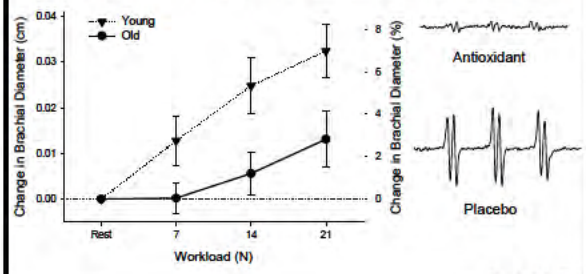
For similar flow/shear, arm blood vessel reactivity during exercise is altered with age



Donato *et al* 2010

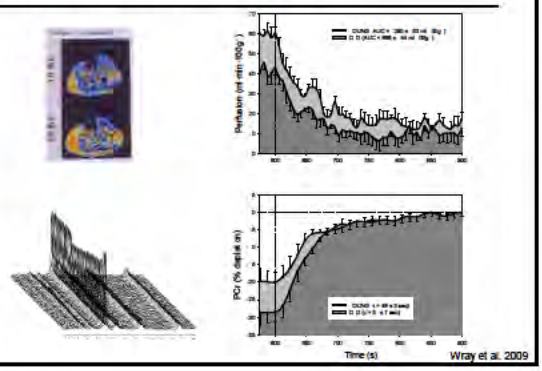
The effect of oral antioxidants on arm vessel reactivity during exercise in the old

AO cocktail: Vitamin C (1,000 mg); Vitamin E (600 I.U.); Alpha-lipoic acid (600mg)



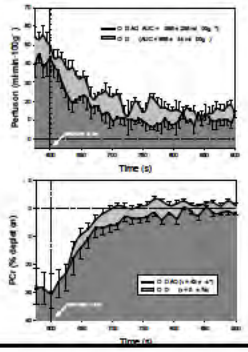
Donato *et al.* 2010

Aging and muscle perfusion
and metabolism assessed by NMR



Wray et al. 2009

Effect of Antioxidants on perfusion
and metabolism in older subjects
assessed by NMR



Wray et al. 2009

Initial Conclusions:

- Aging is associated with attenuated muscle blood flow and vascular reactivity - free radicals originating from muscle or the vasculature may play a role

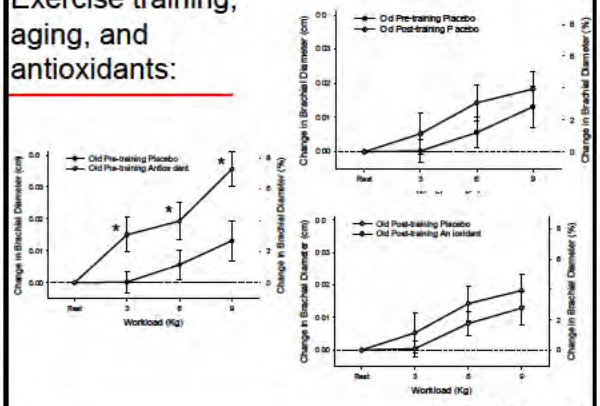
- Antioxidant and exercise induced vasodilation studies with EPR and NMR support the role of free radicals in the attenuated vascular function with age

"Twist in the tail"

Antioxidants:

If two wrongs don't make a right, do two rights make things better?

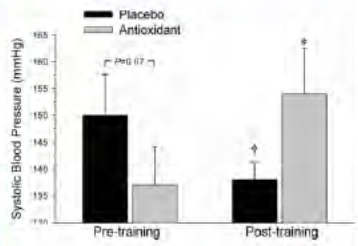
Exercise training, aging, and antioxidants:



Donato *et al. (in preparation)*

Antioxidants: Exercise Training and Blood Pressure

Beneficial effects of exercise training on SBP are negated by AO consumption.

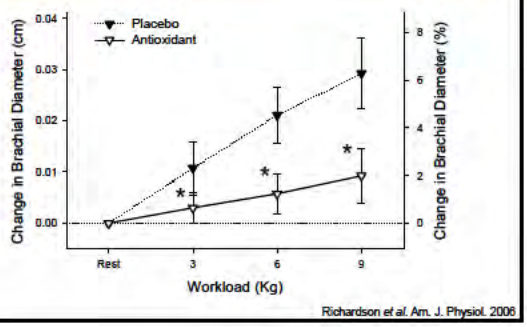


Wray *et al* Clin Sci 2009

"Twist in the tale II"

Antioxidants:
Should you fix what is not broken?

The effect of oral antioxidants on arm vessel reactivity during exercise in the young



Richardson *et al.* Am. J. Physiol. 2006

Conclusions II:

- The balance between pro and antioxidant forces, as a consequence of acute exercise, appears to be influenced by PHYSICAL ACTIVITY and AGE
- In the face of the traditional negative view of oxidative stress these interactions result in somewhat paradoxical results that, in turn, support an IMPORTANT and BENEFICIAL physiological ROLE for FREE RADICALS

Utah Vascular Research Laboratory

The University of Utah
Division of Geriatrics
Department of Exercise and Sports Science

UVRL.org

National Institute of Health
American Lung Association
American Heart Association
Parker B. Francis Foundation
Stein Institute For Aging Research
Tobacco Related Disease Research Program
Association Francaise contre les Myopathies
Office of Rural Health VAMC
Rehabilitation Research and Design VAMC