

The Modern Science of Longevity

By Len Kravitz, Ph.D., lkravitz@unm.edu, www.unm.edu/~lkravitz/

I. Aging

- A. "Aging is an intricate phenomenon characterized by a progressive decline in physiological functions and an increase in mortality, which is often accompanied by many pathological diseases." (Bouzid et al., 2015)
- B. Successful aging: "Absence of disease and disability; high cognitive and physical functioning; and active engagement with life." (Brummel-Smith, 2007).
- C. Species that live longest: Galapagos tortoise (100 plus years); Indian elephant (79 years); Sturgeon (82 plus years).
- D. Oldest person on record: Jeanne Louise Calment. Lived to 122 years; lived in France; took up fencing at 85 yrs, rode a bicycle at age 100; father lived to 93; mother lived to 86

II. Why do we age? Taylor & Johnson. (2008). Physiology of Exercise and Healthy Aging. Human Kinetics

Wear and Tear Theories

Cells, organs, systems of body wear out

Damage from internal and external; Cells lose ability to regenerate

Causes: irritants or pollutants in air, food, smoke; breakdown basic cell processes

Genetic Theories

Genes are programmed from birth to death

Concept of a biological clock; Genes dictate cellular aging; Cellular 'errors' accelerate aging

General Imbalance Theories

We are a 'Yin and Yang' species: Opposite forces that form a whole

Brain, endocrine glands, immune system (or a combination) become 'imbalanced' and then fail

'Dysdifferentiative' Hypothesis of Aging

Pituitary gland, hypothalamus and other regulators of brain are very specialized

Small changes in function result in major functional changes in body

Mitochondrial Free-Radical Hypothesis of Aging

In mitochondria (organelles that are power plants of cell); Accumulation of free radicals

(superoxide and hydroxyl molecules) from cell metabolism; highly reactive free radicals are

produced and damage DNA, cells, and interfere with efficiency of ATP synthesis and organ ages...

Clarity Final Report (2007). What are the 4 biggest fears of aging? 1) Loss of independence (key issues are health, memory & getting around), 2) moving into a nursing home, 3) Loss of family and friends, 4) Giving up driving, NOTE: only 5% fear their own death

III. What factors increase the chance of aging optimally? (Lopez-Otin et al., 2016)

- A. Aerobic exercise
- B. Resistance exercise
- C. Adequate Sleep
- D. Lifestyle (i.e., stress management)
- E. Healthy nutrition choices
- F. Preventive medicine (examinations, immunizations, screening tests, etc.)
- G. Early treatment of disease & medical conditions
- H: Franklin Booth (2012). "Low cardiorespiratory fitness is a sounder predictor of death than risk factors such as hypertension, smoking, and diabetes."

I. CVD, Oxidative stress, Inflammation & Aging: WHO (2016): CVD is #1 cause of death; 31% of all deaths globally; aging leads to development of large artery thickening and stiffness, diminished cardiovascular function due to endothelial dysfunction; reduction/impairment of vasodilators, particularly nitric oxide, development of atherosclerosis

J. Cardiorespiratory exercise has a major effect on vascular endothelial function by improving factors such as vasodilator-to-vasoconstrictor balance, reductions in inflammation and oxidative stress, and growth of new capillaries in skeletal muscle

K. The impairments observed with nitric oxide in the endothelium are minimized and even reduced with cardiovascular exercise

L. Cardiovascular exercise also increases production of specialized cytokines, which are molecular messengers that regulate various inflammatory responses in order to control the body's response to disease and infection.

IV. Shephard, R. J. (2008). Maximal oxygen intake and independence in old age. *British Journal of Sports Medicine Online First*, April 10, 2008, pp 1-19.

- A. A review of 30 studies (since 1990) with male and female subjects age 64 yr or older
- B. Investigated the relationship of aerobic activity, aging and VO₂max (8-10, 12-18, 24-52 wk)
- C. Findings of this review:
- D. Men: VO₂max tends to drop 5 ml/kg/min each decade starting at age 20 (drop from 45 ml/kg/min)
- E. Women: VO₂max tends to drop 5 ml/kg/min each decade starting at age 35 (drop from 38 ml/kg/min)
- F. Decline largely due to physical inactivity and increase in body fat
- G. Once VO₂max drops to 18 ml/kg/min for men and 15 ml/kg/min for women a person loses functional independence
- H. Aerobic activity (50%-70% HRmax; 3-5 times a week; 30 min/day) can retard decline
- I. 8-10 weeks training: VO₂max improves 12.9%
- J. 12-18 weeks training: VO₂max improves 14.1%
- K. 24-52 weeks training: VO₂max improves 16.9%
- L. Higher intensities, 75%-85% HRmax; greater gains (25% increase = increase in 6 ml/kg/min)
- M. Equivalent to gain back 12 years of vigor
- N. New 'buzz word' in exercise science: Cardioprotection
- O. Research from 33 studies with 102,980 men and women shows that with each MET (3.5 ml O₂/kg/min) increase in maximal aerobic capacity there is a 13%-15% DECREASE in risk of cardiovascular disease and all causes of mortality.
- P. BEST HIIT for combatting CVD: 4min bouts of high intensity (85-95% HRmax) {RPE 16-17; Hard} with 3min recovery intervals (RPE 11-12; Light). (Ramos et al., 2015).
- Q. Thomas Jefferson: "Walking is the best possible exercise. Acclimate yourself to walk very fast."
- R. Aerobic Exercise Summary: improves insulin sensitivity, helps prevent diabetes, can reduce CAD risk by up to 50%, lower incidence of colon cancer and breast cancer, can improve balance and prevent falls, weight bearing aerobics will preserve bone mineral density, can help lose and maintain loss of body fat, can lower blood pressure (if elevated), can improve cholesterol and triglyceride levels

V. Melov, S. et al. (2007). Resistance exercise reverses aging in human skeletal muscle. *PLoS ONE*, 2(5): e465.

- A. Some basics
 - 1. Loss of muscle and deficits in strength begin to occur at 40 yr.
- B. The study
 - 1. 26 males and females (ave age = 68 yr), physically active on 3 days/week
 - 2. 25 males and females (ave age = 24 yr), modest physical activity
 - 3. All subjects were non-smokers; no orthopedic limitations; no coronary heart disease
 - 4. Resistance training 2 days/wk for 26 weeks

5. Chest press, leg press, leg extension, leg flexion, shoulder press, lat pull, seated row, calf raise, crunches, back extension, biceps curls, triceps extension
6. Initially trained with single set at 50% of 1 RM and increased to 3 sets at 80% of 1RM
7. Results of muscle biopsies and RNA analysis
8. 179 genes of age and exercise had a reversal of gene expression (functioning better)
9. Gene expressions of the resistance trained older subjects was similar to younger group
10. Mitochondrial impairment, normally seen with inactivity, reversing with 6 months of training
11. “We were very surprised... The fact that their genetic ‘fingerprints’ so dramatically reversed course gives credence to the value of exercise... reversing the aging process”
12. Other benefits of resistance exercise include increase in fat-free mass, in bone mineral density, increase in muscular strength, increase in glucose metabolism, increase in muscular endurance, lower incidence of chronic diseases, improved psychological well-being and increase in resting metabolism.

VI. Lopez-Otin, C. et al. (2016). Metabolic control of longevity, *Cell*, 166, 803-821.

A. Lifestyle strategies for optimal health

1. Physical activity and pace: minimum of 30 minutes/day at a brisk pace
2. Diet: replace saturated and trans fats with unsaturated fats; eat more fruits and vegetables; substitute chicken, fish, nuts/beans for red meats (Mediterranean)
3. Light/moderate alcohol intake (≤ 2 drinks/day)
4. No smoking
5. BMI < 25 (kg/m^2) and/or waist girth: women < 88 cm (35 in), men < 92 cm (36 in)
6. Take Home: Even later in life, combined lifestyle factors are associated with a markedly better improvements in health. Hippocrates, 2,400 yrs ago. “That which is used develops, and that which is not used wastes away... If there is any deficiency in food or exercise, the body will fall sick.”
7. What about sleep? Sleep deprivation is associated with the development of hypertension, obesity, abnormal cholesterol and blood fats, and type 2 diabetes

VII. Stress/Cortisol Aging Connection: Chronic stress activates the HPA axis (hypothalamic-pituitary-adrenocortical axis) which: decreases leptin, increases cortisol, increase grehlin and increases neuropeptide-Y; all are factors increasing brain aging/dementia

Stress/Cortisol/Obesity Connection: Body reacts 3 different ways to stress:

- A. When you feel challenged: Release norepinephrine (fight hormone)
- B. When you feel loss of control: Release epinephrine (flight/anxiety hormone)
- C. When you experience chronic stress: Release cortisol leading to cortisol cascade
- D. Cortisol released from the adrenal cortex of the adrenal glands
- E. Cortisol cascade: 1) Release fatty acids in blood which is a precursor to heart disease, 2) Relocating fat deposits to deep abdomen (visceral obesity), and 3) Enhances lipogenesis or new fat creation (pills do not work to combat this cascade!)
- F. It has been shown that mind-body programs, relaxation techniques, problem solving (at work at home) and exercise lead to less stress, depression and less cognitive decline.

VIII. Affirmation breathing drill to combat stress: “I am in control”; Benjamin Franklin: “To lengthen thy life, lessen they meals.”

IX. What are the longevity hot spots around the world? How do the cultures live? 4 'Blue Zones' in the world where people reach 100 yrs 10 times greater than in U.S. 1) Sardinia, Italy (diet high in vegetables; walk at least 5 miles/day, culture emphasizes laughter and high family value), 2) Okinawa, Japan (diet high in vegetables and fruits), active walkers, strong social groups and emphasis of purpose in life), 3) Loma Linda, CA (Seventh Day Adventist community, diet/health and religion are closely tied, vegetarian diet, emphasize social support and volunteerism) 4) Nicoya Peninsula, Costa Rica (light dinners with corn and beans staple, plenty of fish and vegetables, work hard and have strong sense of purpose, family and community). Commonalities of 4 Blue Zones: physical activity, mission/purpose of living, balance of work/recreation/family, eat less (80% rule), eat more in fruits and vegetables, healthy social network, strong spiritual or religious bond

X. Characteristics of Supercentenarians: Wilcox, D.C. et al. (2008). Life at the extreme limit. Phenotypic characteristics of supercentenarians in Okinawa. *Journal of Gerontology*, 63A(11), 1201-1208. High physical and cognitive function, non-fasting glucose 100-116 mg/dl, total cholesterol <200 mg/dl and dropping, CVD, CAD, stroke, cancer is rare, HDL cholesterol >50 mg/dl, drink moderately or not at all, those who smoked quit at 70 yrs, systolic BP is <120 mmHG, diastolic BP is <74 mmHG, BMI <22, blood fats <100 mg/dl, live 90-95% life very healthy

XI. Yaffe, K, et al. (2009). Predictors of maintaining cognitive function in older adults: The Health ABC Study, *Neurology*, 72, 2029-2035. Keogh, J.W.L, et al. (2009). Physical benefits of dancing for healthy older adults: A Review: *Journal of Aging and Physical Activity*, 17, 479-500. What about the psychosocial contributors to optimal aging?

- A. Create a meaningful social network: greater social companionship is associated with higher general health, mental health and vitality
- B. Volunteering acts as a buffer against stress-related diseases (community/public service, hospital visits, organizations, youth, go back to school). Benefits physical and mental health. Social integration is associated with decreased C-reactive protein, a risk factor of CAD.
- C. Economic prosperity vs. economic deprivation
- D. Start 'dancing with the stars': Dancing can improve aerobic power, lower body muscular endurance, strength, flexibility, balance, agility, and gait speed for older males and females. It will also reduce cardiovascular health risk and can be central in the prevention of falls.

Final Thoughts: Resistance exercise, cardiovascular exercise, mind-body techniques, social engagement, sleep, proper nutrition = optimal aging/healthy aging...GO FOR IT!

Final Quote from Kenneth Cooper: "We do not stop exercising because we grow old – we grow old because we stop exercising.."