

The aging phenotype: organismal and systematic aspects



Reading:
Handbook of
Aging Ch 12,
Immune
System Activity

A&S300-002 Jim Lund

The aging phenotype

Declining function

Diseases of aging

Sleep Disturbances

- Total time sleeping remains constant thru adulthood (daytime naps)
- Rare to have unbroken sleep if over 50
- Less restful
- Dreamless sleep
- Apnea, heartburn, leg movements

Aging vision



- By mid 40s, half of population needs glasses
- Transmission of light in the eye reduced between ages 34-45
- Lens becomes harder and less flexible
- Cataracts 25% over age 75
- Older pupils are smaller than younger
- Acuity declines ages 40-50

Hearing

- Problems increase around age 40; sharply at 60
- Mainly due to loss of hair cells in the inner ear.
- Loss is greater at high frequencies
- Sense of social isolation increases
- Hearing aid reduces low frequencies, limits some sounds, improves others
- Hearing aids used less than glasses

Other Senses

- Taste and smell: Sensitivity decreases
- Bitter tastes last longer
- Temperature: less pain
- Sensitivity to environmental temperature declines, less efficient regulation of body temp.
- Problems with balance, increased chance of falling.

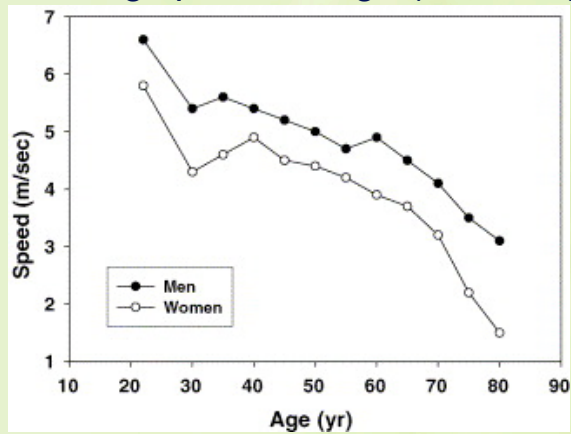
Changes that occur as aging progresses

- Physical performance declines
- Muscle performance declines
- Muscle characteristics (sarcopenia)
- Body composition changes
- Metabolic changes
- Hormonal Changes

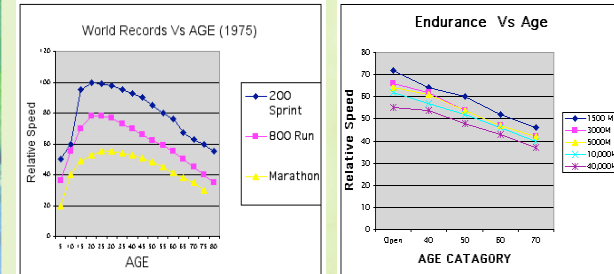
Organismal changes occur

- Total body water decreases with age
 - Mild stresses such as fever or hot weather can create problem
- Increase in reaction time (slowing)
 - Can be improved with physical activity
 - Does not correlate with un-speeded measures of intellectual ability

Running speed vs. age (Humans)

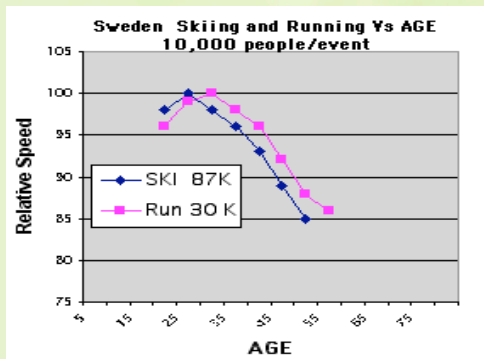


Performance Standard vs AGE



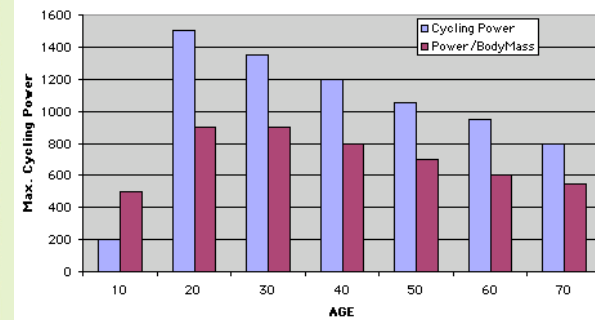
- * Performance standards set by world class athletes
- * D H Moore Nature **253**: 264-5 1975
- * P S Riegel American Scientist **69**: 285-290 1981

Average Performance vs Age



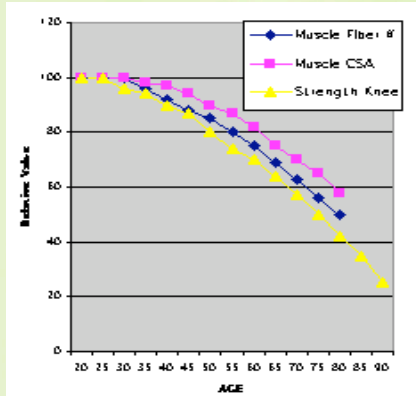
- * Averaging the performance of large numbers of people removes many variables including conditioning and talent.
- * LE Bottiger. Brit. Med. J. **3**: 270-271, 1973

Muscle Performance vs Age



- * Martin et al. J. of Endocrinology 2000
- * Primary determinants of muscle power are volume and sustained pedaling rate (which reflects muscle fiber type)

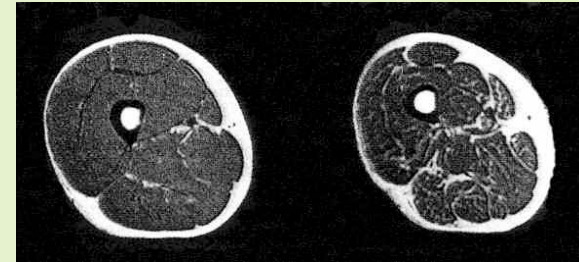
Muscle Characteristics vs Age



- * Muscle Fiber numbers, muscle cross sectional area, and knee extension strength show parallel decline.

* Short KR Nair KS. J. Endocrin. Invest. 22: 95-105. 1999

Muscle loss



Sarcopenia seen in the magnetic resonance image of a cross section of a 25-year-old man's thigh (left) and another age 65 (right). The dark region is muscle, fat appears white.

Changes in Body Composition with Age



- * Lower lean body mass - less muscle

- Reduced protein synthesis

- * Increased Abdominal Fat

- Lower fatty acid oxidation - available fat is stored

* Short KR Nair KS. J. Endocrin. Invest. 22: 95-105. 1999

Body increases with age

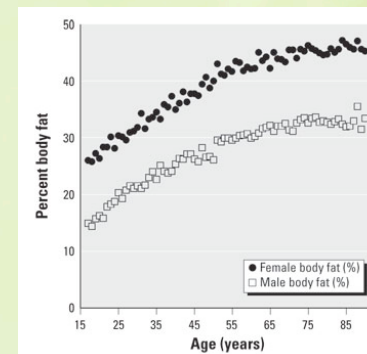
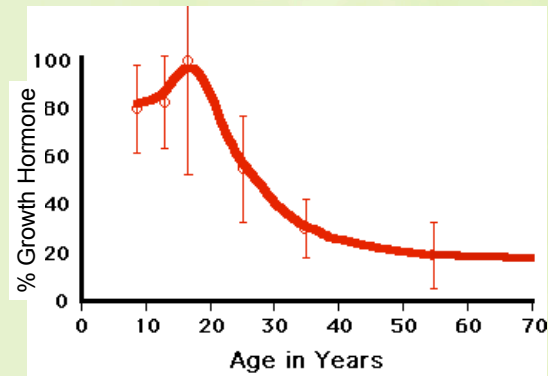


Figure 2. Average percent body fat versus age in men and women: estimates from the National Health and Nutrition Examination Survey III body mass index data using the formulas of Lean et al. (1996).

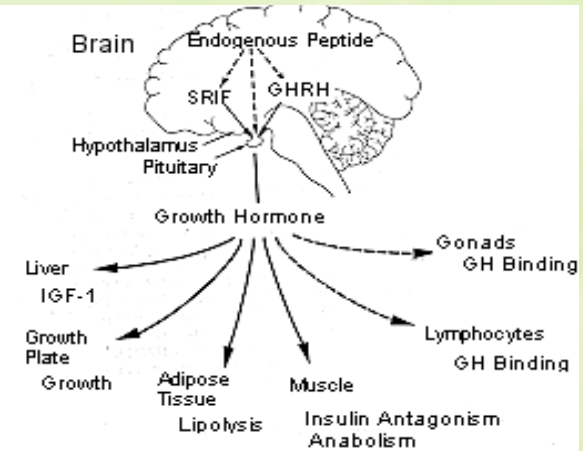
Growth Hormone levels decline



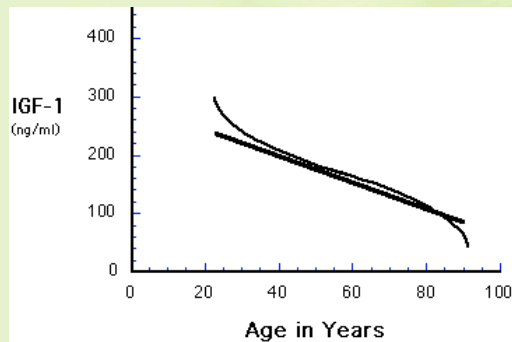
* Level determined by the 24 hr integrated GH concentrations in 80 men and 80 women.

* Zadik et al J. Clin. Endocrin. Metab. 60: 513-516, 1985

Growth Hormone Functions



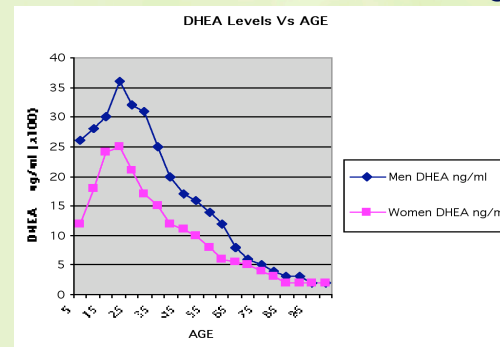
Insulin-like growth factor declines in older animals



* Insulin Like growth Factor is the chief mediator of growth hormone action.

* IGF-1 is produced in the liver in response to GH secretion, also in peripheral tissues.

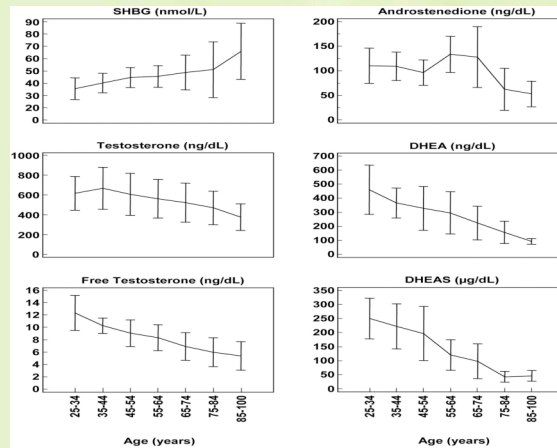
•DHEA levels decline with age



• Regalson W, Colman cC. "The super Hormone Promise" 1997 page 7. Pocket Books, Simon & Schuster Inc.

• DHEA: an adrenal steroid hormone

Serum androgen levels



Reproduction

- ✳ Female: Menopause (full year without menstrual cycle)
- ✳ Male: Changes in levels of testosterone which impacts energy, sexual function.
- ✳ Males can suffer from erectile dysfunction-impotence, with biological and neurological (Parkinson's, dementia) causes.

Functional Consequences of Aging Respiratory System

- ✳ Decreased vital capacity
- ✳ Decreased subglottic pressure
- ✳ Decreased forced expiratory volume
- ✳ Inability to generate stress contrasts
- ✳ Diminished endurance
- ✳ Reduced loudness
- ✳ Smaller phrase units

Structural Changes with Age: Respiratory System

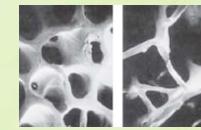
- ✳ Senile kyphosis (Curvature of the Spine)
- ✳ Pleural drying and thinning
 - ✳ Pleural space: the tiny area between the two layers of the pleura (the thin covering that protects and cushions the lungs)
- ✳ Decreased elastic recoil
- ✳ Thoracic muscle atrophy
- ✳ Vertebral degeneration
- ✳ Costovertebral calcification
- ✳ Costovertebral ossification

Physiological Changes in the GI tract

- * Slowing of motility - constipation
- * Atrophic gastritis - 33% over age 60
- * Stomach inflammation, decrease in hydrochloric acid, increase in bacteria
- * Decrease in absorption of B₁₂, biotin, calcium and iron.

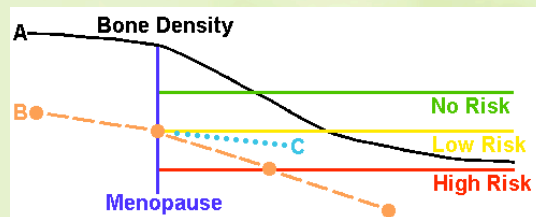
Skeletal Systems

- * Connective Tissue/Collagen. As we age cross links develop and result in tissue that becomes stiff and inflexible. Cross linked collagen produces loss of elasticity, hardened arteries, joint stiffness.
- * Bone degeneration through lack of calcium and protein. Loss of bone mass and density (Osteoporosis).
 - * Very common: >60 years, 1 in 2 women, 1 in 3 men sustain an osteoporotic fracture.



Normal bone Osteoporotic bone

Skeletal Systems



Changes in bone density with aging in women.

The normal curve (A) steepens following menopause. A woman who begins with diminished bone density (B) even before menopause is at great risk. (C) use of diet and exercise regimens can help to slow bone loss.

Aging & the Immune System

- ↓ Immunocompetence
- ↓ Stress response
- ↓ Inflammatory response
 - Infection in older adults is more difficult to detect

Slight & subtle symptoms should be taken seriously!
Older adults often have serious infection without a fever!

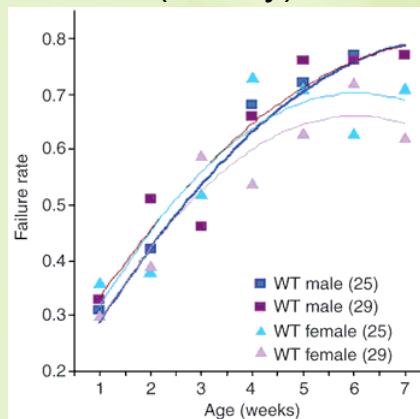
Aging Immune System Changes

- ↓ Effectiveness of physical barriers
- ↓ Cellular (*T-cell mediated*) immunity
- ↓ Humoral (*B-cell mediated*) immunity
- ↓ Inflammatory response
Infection in older adults is more difficult to detect.
Older adults often have serious infection without a fever!

Cardiovascular Disease

- Over age 65--half of all deaths
- Changes in cardiovascular system:
 - Heart needs more time to relax between contractions
 - Less flexible walls of aorta
 - Elastin, collagen, and fat in heart wall increase, muscle decreases
- Women's risk increases after menopause

Heart disease in *D. melanogaster* (fruit fly)



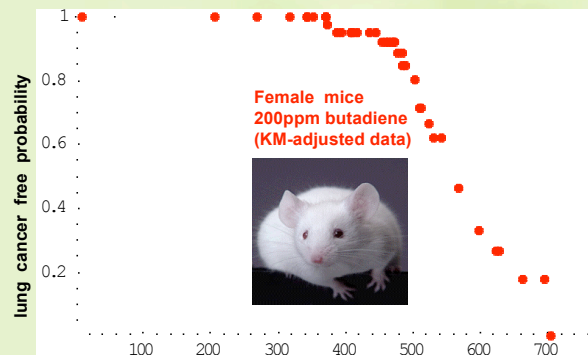
Diabetes type II (insulin-resistant)

Age	Incidence
20–39 years	2.2%
40–59 years	9.2%
60 years and over	19.2%

(1999–2000 data)

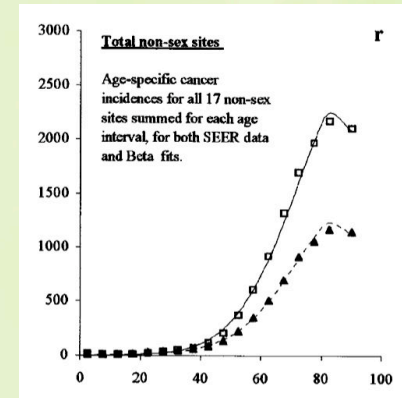
<http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=healthus04.table.333>

Lung cancer in mice



Toxicology and carcinogenesis studies of 1,3-butadiene in B6C3F₁ mice
National Toxicology Program (USA) 1993

Cancer incidence is age-related



Rates per 100,000 individuals, summed over 17 types of cancer.

Limitation of activity caused by chronic conditions

Age	Incidence
18-24 years	4.4%
25-44 years	6.9%
45-54 years	13.7%
55-64 years	21.1%
64-74 years	25.2%
75 years and over	45.1%

(2002 data)

<http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=healthus04.table.334>