

## The aging phenotype: organismal and systematic aspects



A&S300-002 Jim Lund

Reading:  
Handbook of  
Aging Ch 12,  
Immune  
System Activity

## 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.

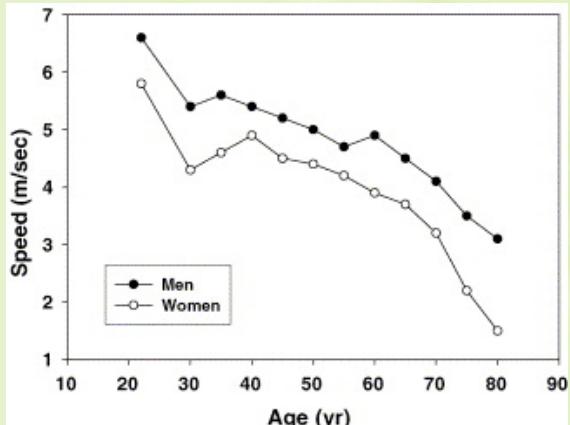
## Changes that occur as aging progresses

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

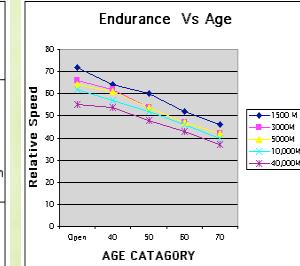
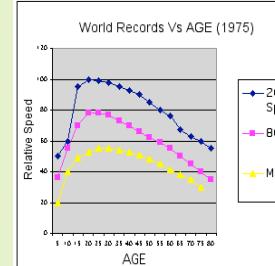
## Organismal changes occur

- 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

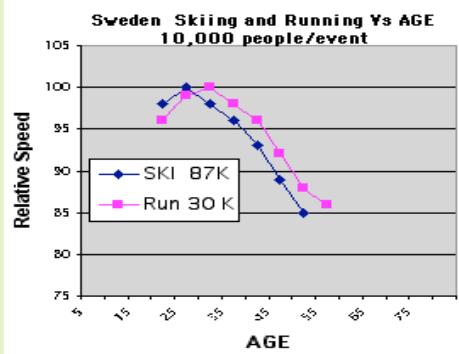


\* Performance standards set by world class athletes

\* D H Moore Nature 253: 264-5 1975

\* P S Riegel American Scientist 69: 285-290 1981

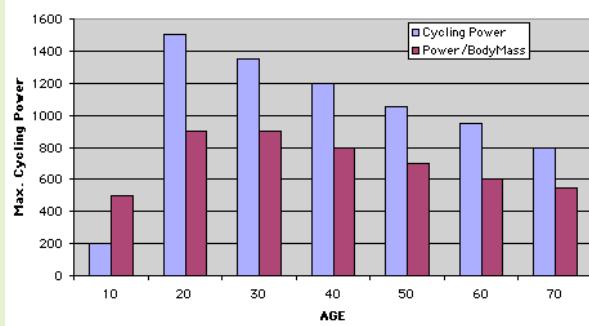
## Average Performance vs Age



\* Averaging the performance of large numbers of people removes many variables including conditioning and talent.

\* LE Bottiger. Brit. Med. J. 3; 270-271, 1973

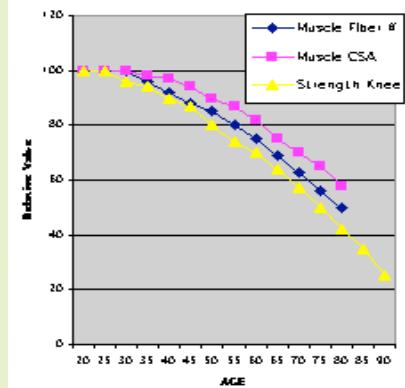
## Muscle Performance vs Age



\* 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



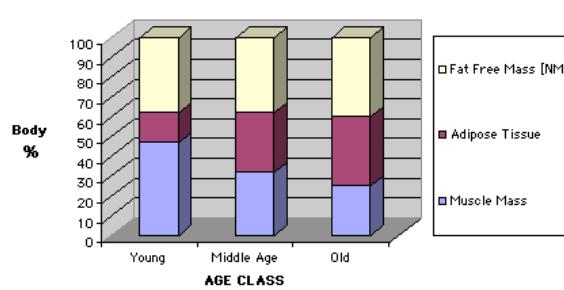
- \* Muscle Fiber numbers, muscle cross sectional area, and knee extension strength show parallel decline.
- \* Short KR Nair KS. J. Endocrin. Invest. 22: 95-105. 1999

## 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

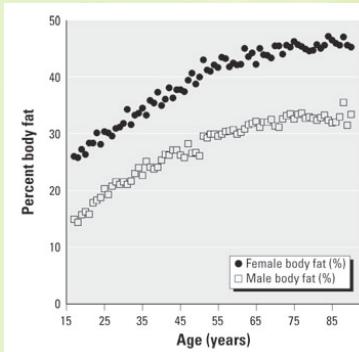
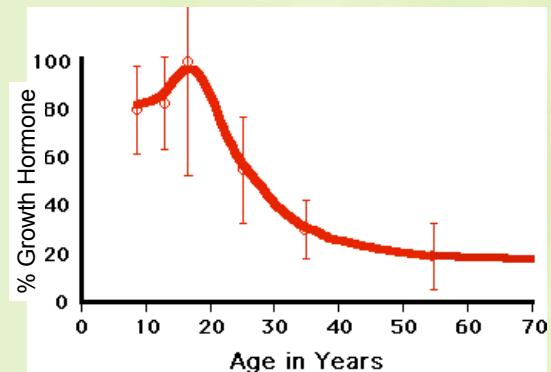


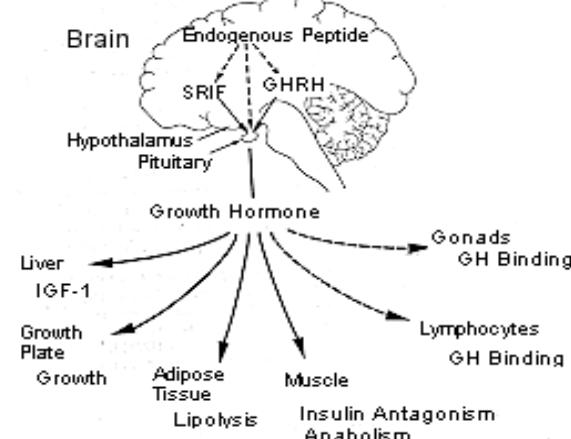
Figure 2. Average percent body fat versus age in men and women: estimates from the National Health and Nutrition Examination Survey III body mass index data using the formulas of Lean et al. (1996).

## Growth Hormone levels decline

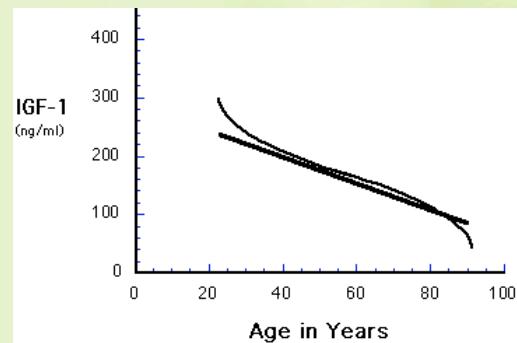


- \* Level determined by the 24 hr integrated GH concentrations in 80 men and 80 women.
- \* Zadik et al J. Clin. Endocrinol. Metab. 60: 513-516, 1985

## Growth Hormone Functions

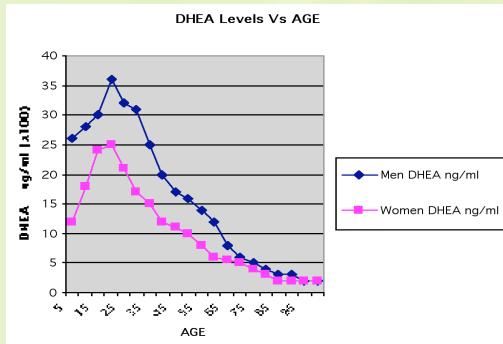


## Insulin-like growth factor declines in older animals

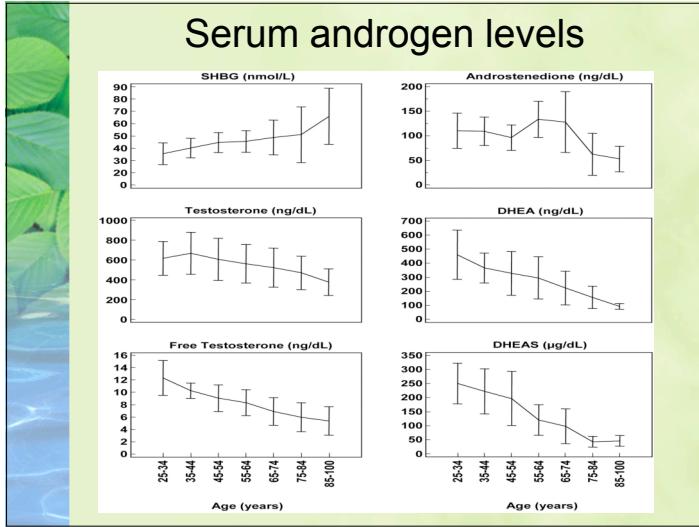


- \* Insulin Like growth Factor is the chief mediator of growth hormone action.
- \* IGF-1 is produced in the liver in response to GH secretion, also in peripheral tissues.

## DHEA levels decline with age



- Regalson W, Colman C.C. "The Super Hormone Promise" 1997 page 7. Pocket Books, Simon & Schuster Inc.
- DHEA: an adrenal steroid hormone



## 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

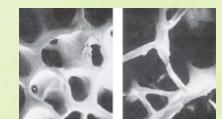
- ✿ Senile kyphosis (Curvature of the Spine)
- ✿ Pleural drying and thinning
  - ✿ Pleural space: the tiny area between the two layers of the pleura (the thin covering that protects and cushions the lungs)
- ✿ Decreased elastic recoil
- ✿ Thoracic muscle atrophy
- ✿ Vertebral degeneration
- ✿ Costovertebral 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 B<sub>12</sub>, biotin, calcium and iron.

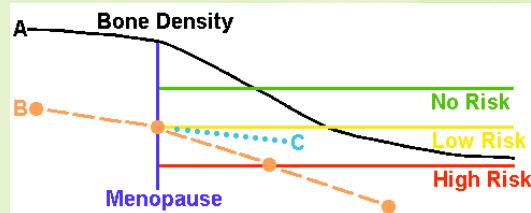
## Skeletal Systems

- 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!

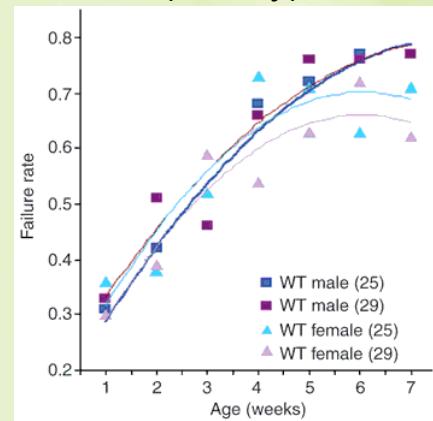
## Aging Immune System Changes

- ↓ 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)

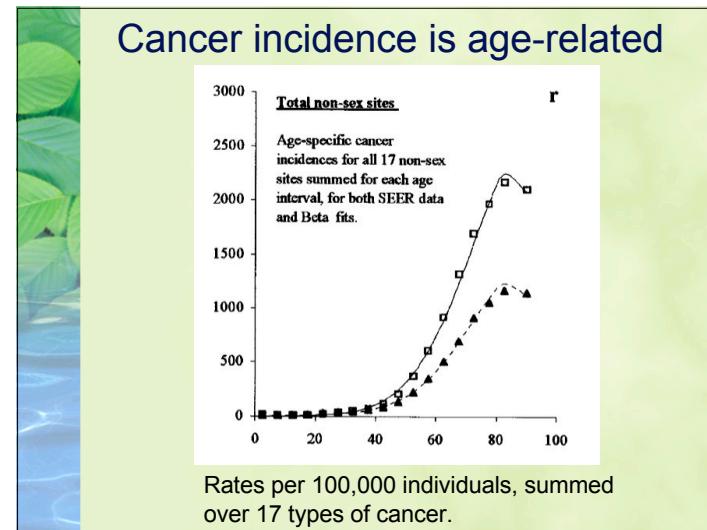
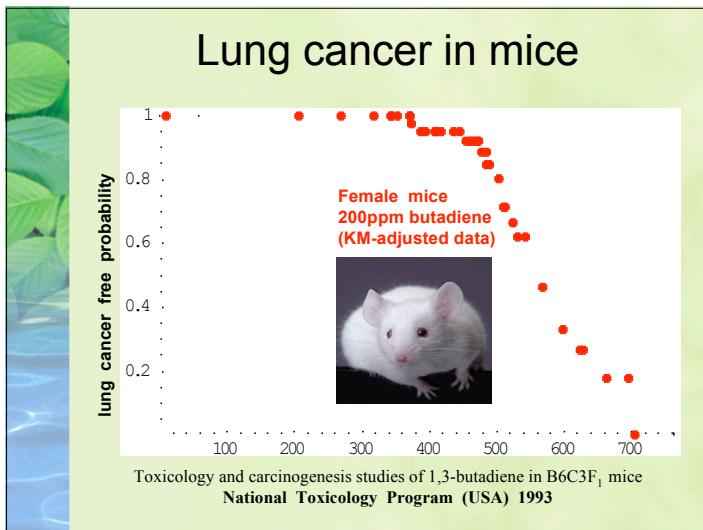


## Diabetes type II (insulin-resistant)

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>



### 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>