Aging and Disease Processes

BIO 375
Pathophysiology

The Aging Process

- Aging begins at birth but becomes more obvious after age 30
- Senescence refers to the period of life from old age to death
- Effects of aging vary from person to person and do not necessarily parallel chronological age
- Today, more people are living longer
  - Life span
  - Life expectancy

Today's longer life is due primarily to:
- Improved social and living standards
- Improved nutrition
- Better health care

Aging is a natural part of life, BUT...
- Degenerative changes associated with aging can predispose a person to certain pathologies, AND
- Pathologic changes can hasten aging
Gerontology

- A lot of research is taking place into the physiological changes related to aging in hopes of:
  - Delaying these changes
  - Treating them
  - With aging, there is a general loss of function at the cellular and organ level and the body shows a decreased capacity to adapt to change

Theories of Aging

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Hayflick Limit and Telomeres

- Leonard Hayflick (1969) noted that cells grown in tissue culture had a finite number of cell divisions before becoming senescent and dieing out.
- Telomers at the ends of chromosomes get progressively shorter with each mitosis and when completely gone, cells are unable to divide
- Cancer cells are immortal and are able to maintain their telomers
Tissue Changes with Aging

- Cells assume less organized arrangements in tissues later in life
- Elastic fibers are lost
- Collagen cross-linking increases
- Mitosis gradually slows down
- Metabolism slows and tissue repair lags
- Neurons and muscle cells cannot reproduce and their loss reduces function
- Some cells accumulate wastes
- Changes lead to increased risk of cell death, cancer or other diseases

Significant Functional Changes with Aging

- Hormonal changes
- Reproductive changes
- Cardiovascular changes
- Musculoskeletal changes
- Respiratory changes
- Neurologic changes
- Gastrointestinal changes
- Urinary system changes
- Other factors including infections

Hormonal Changes

- Hormone secretions tend to remain relatively constant into old age, BUT
  - Number of cell receptors may decrease
  - This diminishes the body’s response to these hormones, e.g. Type II Diabetes mellitus
- The major natural hormonal change occurs in women at menopause around age 50
  - Ovaries stop secreting estrogen and progesterone
  - Pituitary levels of FSH and LH rise
- In males there is a decline in testosterone
Reproductive System Changes

- **Menopause** refers to the change that occurs in women at about age 50
  - Ovaries cease to respond to FSH and LH, resulting in:
    - Failure to ovulate
    - Cessation of the menstrual cycle
    - Declining levels of estrogen and progesterone
  - Low hormone levels cause thinning of the lining, loss of elasticity and decreases in secretions of the vagina and cervix

These changes may cause painful intercourse

- Vagina becomes more alkaline, predisposing older women to recurrent vaginal infections
- Breast tissue decreases in volume
- Hot flashes may occur causing:
  - Periodic sweating and vascular disturbances
  - Headache, irritability or insomnia

Changes in Older Males

- Testosterone levels gradually fall
  - Testes decrease in size
  - Sperm production is reduced
  - Secretions of prostate decrease
- **Benign prostatic hypertrophy** (BPH) which can decrease urine flow
Other Reproductive Changes

- Cancer of the reproductive organs is more common in old age in both sexes:
  - Prostatic cancer in males
  - Uterine and breast cancer in females

Cardiovascular Changes

- Age related changes in cardiac muscle and connective tissues of the heart include:
  - Fatty tissue and collagen fibers accumulate in the heart and may lead to:
    - Interference with impulse transmission
    - Decrease in cardiac muscle contraction
  - Size and number of cardiac muscle cells decreases reducing strength of contraction
  - Heart muscle cells cannot reproduce

- Heart valves often thicken and become less efficient
- Cardiac output and cardiac reserve are often reduced
- Proper nutrition and a regular exercise program can help slow these changes
Blood Vessel Changes
- Loss of elasticity and accumulation of collagen results in thickening of the walls limiting expansion and reducing the size of the lumen in small arteries
- These changes lead to arteriosclerosis
- Degenerative changes also promote the accumulation of cholesterol and lipid in blood vessel walls called atherosclerosis
- These lipid plaques obstruct blood flow and predispose to thrombus formation

Musculoskeletal Changes
- Osteopenia is the typical gradual loss of bone mass with advancing age
- Osteoporosis refers to loss of bone mass serious enough to compromise bone structure resulting in easy fractures (crush fractures and broken bones)

Risk Factors of Osteoporosis
- Hereditary predisposition
- Decreased estrogen levels
- Decreased weight bearing activity or stress on bone (sedentary life style or immobility)
- Decreased calcium intake or absorption at all ages, including childhood
- Decreased osteoblastic activity perhaps due to glucocorticoid/cortisol use
Bone Structure: Cortical and Trabecular components

The outer surface of bone consists of dense bone called cortical bone; the interior is called spongy or trabecular bone.

Bone Loss from Cortical and Spongy Bone

- Quantity of bone matrix decreases with aging because the rate of bone loss exceeds the rate of formation
  - Begins in some people by age 20
  - By 30 most people are losing bone mass
  - By 35 rate of loss is substantial
    - First, only trabecular bone is lost
    - Cortical bone loss is detectable by age 40
  - Bones that are mostly trabecular bone are most likely to suffer most and fracture first, e.g. vertebral bodies and the neck of femur

Kyphosis due to Crush Fractures of the Spine

The vertebral body is largely composed of trabecular bone which is lost first and at the fastest rate. This can cause spontaneous crush fractures.
Vertebral Crush Fracture

Prevention of Osteoporosis

- Prevention only real solution
  - Exercise in youth to build bone mass; maintain exercise regimen throughout life
  - Adequate diet including adequate calcium and vitamin D and fluoridated water
  - Adequate sleep (bone building activity increased at night with release of growth hormone)
  - Estrogen replacement after menopause
  - Drugs like Fosamax which inhibits bone resorption

By building bone mass in youth and maintaining bone mass longer, osteopenia may not continue to develop into osteoporosis
Osteoarthritis

- This refers to a degeneration of joint cartilage
- The articular cartilage becomes thin and erosions occur
- This impairs movement and causes pain
- Bones spurs sometimes form increasing pain and further restricts movement
- May require joint replacement

Herniated Intervertebral Disc

- The fibrocartilage in the intervertebral discs degenerate with age
- Sudden stress on the back may herniate the disc:
  - The puts pressure on spinal nerves
  - Cause severe back pain
- Thinning of the discs also causes loss of height

Age Effects on Vertebral Disks

- Vertebrae
- Spinal cord
- Intervertebral disk
- Nucleus pulposus
  - Nerve root
  - Spinous process
- Fusion
- Narrow intervertebral space
- Concave vertebral body
- Loss vertebral tone
- Spinal nerve
- Intervertebral foramen
- The vertebral spinous process
- The vertebral body
- The vertebral articular process
- The vertebral arch
Other Musculoskeletal Changes

- Skeletal muscle mass declines with age
  - Due to atrophy
  - Due to loss in number of fibers
- Loss of muscle and cutaneous tissue leads to increased susceptibility to skin breakdown and pressure related ulcers
- Muscle strength decreases but depends on activity level of the individual
- Flexibility decreases from loss of elastin

Movements tend to get slower

Several things contribute to this:
- Increased stiffness
- Reduced coordination and balance
- Due not only to changes in bones, joints and muscle, but to neurological changes
- Regular exercise and good nutrition can greatly help in slowing these changes

Respiratory Changes

- Compliance decreases with aging for several reasons:
  - Elasticity in tissue is reduced
  - Costal cartilages calcify reducing rib movement
  - Intercostal muscles atrophy and weaken
  - Other skeletal changes (e.g. rib shape) may reduce thoracic movement
Several volume measurements reduced affecting breathing:
- Decreased expansion for deep breathing
- Decreased expiratory reserve volume
- Decreased vital capacity

Skeletal muscle weakness also reduces cough effectiveness
- Secretions tend to accumulate
- Risk of pneumonia increases

Vascular degeneration in the lungs leads to decreased perfusion and reduced gas exchange in the alveoli
- There tends to be a reduced oxygen level rather than increased carbon dioxide level
- Oxygen therapy may be helpful
Neurological Changes

- Neurons are not replaced after birth
  - Results in loss in brain mass
  - Loss occurs in different areas and at different rates
  - There is a considerable reserve of neurons
- Rate of loss affected by:
  - Toxic materials like lead can hasten loss
  - High levels of mental activity all during life may assist in maintaining brain function

Degenerative Changes in Nerve Tissue Includes:

- Lipid accumulations
- Loss of myelin sheath
- Development of abnormal neurofibrils and plaques on the cells (especially seen in Alzheimer’s disease and senile dementia)
- Vascular impairments such as arteriosclerosis
- Decreased cellular response to neurotransmitter chemicals leading to delays in synaptic transmission

Functional Changes include:

- Slower response time
- Decreased reflexes
- Short-term memory lapses
- Autonomic nervous system does not always provide adequate adaptation resulting in decreased tolerance to extreme temperatures
- Reduced sensitivity in the skin when touching hot or cold objects
On the other hand:

- Elderly can learn new material and skills, although the process is slower
- With losses of neurons in the brain, those remaining “rewire” themselves around the losses

Changes in the Special Senses: The Eye

- Iris and associated muscles degenerate reducing light accommodation
- Reduction in the reabsorption of aqueous humor increases intraocular pressure and glaucoma
- Lens yellows and becomes less transparent leading to cataracts
- Lens gets less elastic reducing the ability to adjust focus, presbyopia
- Vascular changes in retina can lead to loss of rods and cones leading to vision loss

Changes in the Special Senses: The Ear

- Loss of hearing can be due to either conduction failure through the middle ear or nerve degeneration in the inner ear (conduction vs sensorineural)
- Becomes harder to hear spoken words especially in noisy environments
- Becomes more difficult to determine the source of sounds.
Changes in the Special Senses: Taste and Smell

- The chemical senses diminish with aging
- Taste may be reduced as salivary secretions diminish with aging
- Loss in ability to discriminate between different odors
- Loss of taste and smell may impair appetite and nutrition

Gastrointestinal Changes and Nutrition

- Maintenance of good nutrition may be a problem in some elderly:
  - Older people may think less food is needed as they age and they eliminate important components like protein and vitamins
  - Loss of teeth makes eating more difficult
  - Decreased salivation from aging and some medications reduces taste of food and makes swallowing more difficult
  - Need for soft diet or financial problems limit choices

- Obesity is common in some elderly people who are sedentary
- Obesity increases cardiac stresses
- Likely to lead to atherosclerosis and hypertension
- Gallstones are a complication of obesity
- Type II diabetes in more common in the obese
- Osteoarthritis affecting the weight bearing joints complication of obesity
Decreased secretions of the GI tract reduces digestion and absorption of nutrients
- Absorption of vitamin B₁₂, calcium and iron may be impaired
- Decreased mucus predisposes older people to peptic ulcers
- Decreased motility of the GI tract may predispose to constipation

Malignancies of the GI tract, especially of the stomach and colon are more common in the elderly
- Carcinogenic substances in the diet are more hazardous when associated with constipation since they spend more time in contact with the tissues
- Chronic constipation frequently leads to hemorrhoids and diverticulosis.

Urinary System Changes
- Kidney function decreases in the elderly because of:
  - Loss of glomeruli
  - Degeneration of renal tubules
  - Deteriorating blood vessels
- There is reduced ability to compensate for rapid changes in electrolytes and acids
- There is a reduced capacity for excreting drugs and so blood levels may become excessively high
**Effects on Bladder and Urethra**
- Muscles of bladder and urethra weaken resulting in:
  - Reduced bladder capacity
  - Incomplete bladder emptying
  - Frequent nocturnal micturition
  - Bladder infections
  - Incontinence

**Other Factors**
- Infections are common in the elderly:
  - Due to poor circulation which impairs normal defense mechanisms
  - Tissue healing is impaired by decreased mitosis
  - Slower response of the immune system
  - Skin breakdown and ulcers may predispose to infection
  - Urinary tract infections are more common

**Immune System Problems**
- Cancer is more common in the elderly because the immune system becomes a less effective surveillance unit
- Older people have had a higher cumulative exposure to carcinogens
- Autoimmune disorders are more common like rheumatoid arthritis
Medication Interactions

- Many elderly people take a large number of medications, both prescription and over the counter types
- These combinations lead to the likelihood of undesirable interactions
- With age the levels of drugs tend to rise due to diminished kidney and liver function
- With decreased receptor sensitivity the activity of drugs may diminish with age
- Should periodically reevaluate drugs used, dosage and combinations for interactions