AGE-ASSOCIATED PHYSIOLOGIC CHANGES

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Introduction

- Aging
  - Progressive and broadly predictable changes
  - Increased susceptibility to many diseases
- Organs in the same person age at different rates influenced by
  - Genetic makeup
  - Lifestyle choices
  - Environmental exposures

HEMATOPOIETIC SYSTEM

- Bone marrow mass ⬇
- Fat in the bone marrow ⬆
- Hematopoietic functional reserves ⬇

- The compensatory hematopoietic response to phlebotomy, hypoxia, and other challenges is delayed and less vigorous in the older person
  - This is due to changes
    - to populations of progenitor cells
    - to the bone marrow environmental matrix

- Age is a significant risk factor for **myelotoxicity** due to chemotherapy regimens for malignancies

GASTROINTESTINAL TRACT

- The overall effects of aging on the gastrointestinal system are modest
- Aging itself does **not** cause malnourishment

- Oropharynx
  - The epithelial lining of the oral mucosa thins
  - The gums recede, exposing the tooth cementum, which is more prone to decay
    - Predisposing older persons to root caries and incomplete mastication
  - Edentate patients are at greater risk for inadequate nutritional intake compared with those with partial or full retention of their teeth

- Modest age-associated changes occur in the salivary glands
  - A small decrease in the number of acinar cells
  - Up to a 50 percent decrease in maximal saliva production from parotid salivary glands

- Although accessory salivary gland production is unchanged, fatty infiltration of these glands increases with age
  - Making the discrimination between Sjögren's syndrome and age-associated dry mouth more dependent on the extent of fibrosis than fat

- Up to 50 percent of older patients have subjective complaints of dry mouth, which can impact chewing and swallowing
- Transfer of the food bolus to the pharynx is altered in the majority of older patients
- Loss of esophageal muscle compliance results in increased resistance to flow across the upper esophageal sphincter

- Up to 60 percent of older patients without dysphagia have abnormal transfer to the pharynx on videofluoroscopy
- The strength and coordination of the tongue is impaired in healthy 80-year-old individuals
- Less effective mastication and decreased food clearance from the pharynx lead to increased aspiration risk in older adults

- Esophagus
  - Anatomic changes in the esophagus
    - Hypertrophy of the skeletal muscle at the upper third
    - Decrease in myenteric ganglion cells that coordinate peristalsis
    - Increased smooth muscle thickness

- The amplitude of esophageal contractions during peristalsis decreases, but the movement of food is not impaired
- Abnormal peristalsis after swallowing and non-peristaltic repetitive contractions
  - Attributed to old age and called "presbyesophagus," are now thought to be due to disease processes.

- Secondary contractions contribute to clearance of refluxed food or acid
  - Diminution of these contractions, combined with decreased lower esophageal sphincter tone, results in increased gastric acid exposure

- Secondary esophageal contractions induced by esophageal distention and acid infusion into the esophagus appear to be greatly reduced with age

- Many older patients with severe reflux esophagitis seen at endoscopy have surprisingly little symptomatology

- Stomach
  - Early studies suggested that gastric acid production decreased dramatically with age, with a decrease in parietal cells and an increase in interstitial leukocytes
  - Subsequent studies challenge those findings and suggest that 90 percent of people aged 65 and over are able to acidify gastric contents in the basal unstimulated state

- Over 50 percent of older people are infected with H. pylori, with the prevalence increasing with advancing age

- Increased rates of gastritis and increased sensitivity to gastric irritants, such as nonsteroidal antiinflammatory medications or bisphosphonates, in older adults may be related to several age-related physiologic changes:
  - Decreased prostaglandin synthesis
  - Decreased bicarbonate and nonparietal fluid secretion
  - Delayed gastric emptying
  - Impaired microcirculation

- Gastric motility is determined by the combined effects of the enteric nerves, smooth muscle, and the interstitial cells of Cajal
- The number and volume of the interstitial cells of Cajal bodies decreases by over 10 percent per decade in normal people without motility complaints

- Small intestine
  - The small intestine undergoes modest anatomic changes
    - Moderate villus atrophy and
    - Coarsening of the mucosae
  - The absorption of several micronutrients (eg, xylose, folic acid, B12, copper) may decrease with age but remain adequate for homeostasis

- The efficiency of calcium absorption from the gut lumen decreases because of
  - Decreased vitamin D receptors in the gut
  - Decreased levels of circulating 25(OH) vitamin D
- Women over age 75 absorb 25 percent less of a given dose of calcium than younger women, especially if there is reduced acid secretion

- Iron may also be less well-absorbed, but overall aging impacts the absorption of macronutrients minimally
- Consumed carbohydrates result in significantly more hydrogen excretion in the older adults, suggesting
  - malabsorption and subsequent bacterial metabolism of the carbohydrate in the aging gut

- Up to 15 percent of residents in senior congregate housing have evidence of bacterial overgrowth as assessed by breath hydrogen testing
- Bacterial overgrowth and associated malabsorption can affect nutritional status and micronutrient absorption
- The barrier function of the small intestine may be compromised and local inflammation activated in response

- Decreases in sensory and myenteric neurons contribute to the increased frequency of painless ulcers with increased age

- Small intestinal transit time (measured with capsule endoscopy) seems to be unchanged by age

- Large intestine
  - Anatomic changes with aging in the large intestine
    - Mucosal atrophy
    - Cellular and structural abnormalities in the mucosal glands
    - Hypertrophy of the muscularis mucosa
    - Atrophy of the muscularis externa

- Functional changes
  - Altered coordination of contraction
  - Increased opioid sensitivity that may predispose the older person to drug-induced constipation

- Colonic propulsive motility is reduced with age and about one-fourth of those over 65 years suffer from chronic constipation

- One factor contributing to reduced motility is
  - An age-related reduction in myenteric plexus neurons and a decline in the interstitial cells of Cajal similar to that seen in the stomach

- Intrinsic sensory neurons that respond to physicochemical changes may degenerate disproportionately compared with motor enteric neurons

- The loss of sensory input into local reflex pathways could contribute to reduced propulsive motility
- The loss of intrinsic sensory neurons may also contribute to the decreased visceral response, including decrease in perceived pain with bowel perforation, distention, or ischemia
- As an example, the rigid surgical abdomen after appendiceal perforation is a less frequent finding in those over 75, leading to delayed diagnosis

- Older women may be more predisposed to fecal incontinence than older men as
  - The resting pressure and squeeze pressure decrease with age, resulting in decreased anal sphincter tone
- The internal anal sphincter of continent older people is thickened, perhaps to compensate for decreased resting and maximum pressures in the anal canal with age
- Thinning of the external sphincter correlated with fecal incontinence more than age

- Diverticula are common in Western populations over age 65, with prevalence ≥65 percent.
- The prevalence of diverticula is lower in other populations, presumably with other diets, but nonetheless there remains a strong age-dependence
- The formation of colonic diverticula is attributed to
  - Decreased muscle wall strength
  - Decreased bowel wall compliance
  - Increased intraabdominal pressure required for stool excretion

- Slower large bowel transit and increased segmental contractions (as opposed to propulsive contractions) result in
  - Increased water reabsorption,
  - Leaving harder stools and
  - Increasing the likelihood of wall failure

- The risk of colon cancer increases with age
- In addition to prolonged exposure to potential carcinogens, aging is associated with increased proliferation and decreased apoptosis in the colonic mucosa

- The barrier function of colonic epithelium may be compromised and has been implicated in promoting the proinflammatory state, “inflammaging.”
- Barrier function for lactulose and sucrose is preserved in healthy 65- to 75-year-old persons
- The gut microbiome changes with healthy aging and with age-associated diseases

- Hepatobiliary system
  - Liver mass decreases between 20 and 40 percent with age
  - Liver perfusion and blood flow decreases up to 50 percent between the 3 rd and 10 th decades of life
  - Lipofuscin accumulates in hepatocytes with age and is also seen in young patients with severe malnutrition, accounting for an appearance that has been described as "brown atrophy"

- Older livers have more macrohepatocytes (large cells) and increased polyploidy
- The number of mitochondria per cell increases with age
- The older liver is less tolerant of ischemia which increases the risk of using older livers for transplantation

- Function and anatomy of the gall bladder are well preserved in old age
- The bile composition has a higher lithogenic index, predisposing the older person to cholesterol gallstone formation

- Exocrine pancreas
  - Only modest alterations with age
  - Minor atrophic and fibrotic changes have essentially no impact on pancreatic exocrine function
  - The fat fraction of the pancreas increases with age in healthy women
  - Noninvasive pancreatography indicates
    - Main pancreatic duct dilatation
    - Greater incidence of cysts and side branches of the pancreatic ducts
    - Decrease in stimulated pancreatic flow with advancing age

THE RENAL SYSTEM

- Renal mass decreases by 25 to 30 percent between the ages of 30 and 80 years, with the steepest decline after age 50
- Fat and fibrosis replace some of the remaining functional parenchyma
- Loss occurs primarily in the renal cortex and preferentially affects those nephrons most important to maximal urine concentration

- Normal aging is associated with a reduction in functional glomeruli of almost 50 percent
- Atrophy and resorption of nephrons may contribute to the age effect more than diffuse sclerosis of glomeruli
- The remaining glomeruli have impaired filtering ability, though single nephron studies showed preserved filtration rate until age 70

- Intrarenal vascular changes
  - Spiraling of the afferent arterioles
  - Narrowing of the larger arteries
  - Intimal fibrosis
  - Shunts between afferent and efferent arterioles allowing blood flow to bypass the glomeruli

- Renal plasma blood flow is 40 percent lower in healthy normotensive older men than in young men, and this difference is magnified under conditions that stimulate renal vasodilation

- The older kidney is more prone to nephrotoxicity related to medications, chemotherapy, or intravenous contrast

- The injured older kidney is less likely to recover from acute insult
- The older kidney is also more vulnerable to ischemic insult, with a greater number of cells undergoing apoptosis following ischemia than in the young kidney

- Tubular cells appear to have diminished ability to entirely repopulate the tubules after an acute ischemic insult
  - Potentially an effect of the increasing senescent cell population of the aging kidney

CARDIOVASCULAR SYSTEM

- Advancing age increases the risk for hypertension and coronary artery disease
- The prevalence of coronary artery disease at autopsy may reach 75 percent after the sixth decade in men and two decades later in women
- Many older people perform little physical activity.
- Physical exercise may mitigate some of the age-related changes.

- Modest anatomic changes occur in the right side of the heart
- Right atrial volume increases modestly
- Mean and peak systolic blood flow in the superior and inferior vena cavae decrease with age

- The left atrium enlarges and the left ventricle stiffens with aging
- Left atrial volume, corrected for body size, increases roughly 50 percent from the third decade to the eighth

- The left ventricle also hypertrophies with age, with an average increase in left ventricular wall thickness of 10 percent
- In healthy women, the left ventricle end diastolic volume decreases by 10 to 15 percent from age 20 to age 80
- Both the aortic valve and mitral annulus thicken and develop calcific deposits

- Mitral annular calcification may predispose the older person to cardiac conduction problems
- Ventricular cardiomyocytes hypertrophy, in part as a response to the increased afterload produced by large artery stiffening
- Loss of myocytes with age has been reported to occur by both apoptosis and necrosis
- The total number of cardiomyocytes may be reduced significantly in healthy human hearts

- the loss of myocytes is compensated for by cell hypertrophy, with no net loss in cardiac mass
- Substantial cellular dropout occurs in the sinoatrial (SA) node and more modest cellular loss at the atrioventricular node
  - This may underlie increased sensitivity of the older SA node to calcium channel blockers

- Negligible age-related decrease in the resting heart rate
- Marked decrease in the maximum heart rate in response to exertion or other stressors

- The intrinsic heart rate (the rate without sympathetic or parasympathetic input to the heart) decreases by five to six beats per minute each decade.
- The response to both parasympathetic antagonists (atropine) and beta-adrenergic agonists (isoproterenol) is decreased in healthy older people

- Resting LVEF is not changed in healthy older people, but there are smaller increases in LVEF in response to exercise
- Mortality and the probability of developing heart failure after a myocardial infarction increase dramatically with age

- While myocardial infarction is not a part of normal aging, response to this systemic challenge is impaired because of the aging process
- The aorta increases in diameter, with the upper limits of normal increasing by approximately 5 mm from age 20 to 40 compared with those over 60
- Length increases a few cm from age 20 to 80

RESPIRATORY SYSTEM

- Aging, in the absence of additional challenges, does not result in hypoxia or pneumonia
- Age-related anatomic and functional changes in the respiratory system contribute to the
  - Increased frequency of pneumonia
  - Increased likelihood of hypoxia
  - Decreased maximum oxygen uptake

- Alveolar ducts enlarge due to
  - Loss of elastic tissue
  - Alterations in the supporting network of collagen fibers
  - ❖Resulting in a decreased surface area for gas exchange
- About one-third of the surface area per volume of lung tissue is lost over the life span
- Anatomic dead space ⬆

- Surfactant composition : altered by age
- Alveolar fluid
  - Greater content of proinflammatory proteins
  - Reduced antiinflammatory profile
- Lung angiotensin-converting enzyme 2 (ACE2) expression (the severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2] virus receptor) **increase** with age

- Age increases ventilation-perfusion mismatching because
  - Airways in dependent portions of the older lung, areas that are better perfused than elsewhere, are closed during all or part of the respiratory cycle
- This is a critical factor in the declining arterial PO_2 with age

- The decrease in arterial PO2 (PaO2)
  - May not be linear
  - Decline from age 30 until 70 or 75 and thereafter remains almost constant
- While age-related changes do not result in hypoxia at sea level, older adults may approach hypoxia at altitude
- The fall on PaO2 is slightly greater in women than men

- Carbon dioxide excretion is not impaired with age; changes in $PaCO_2$ are due to disease and should not be attributed to age alone
- Increased stiffness of the chest wall predominates over an increase in compliance of the lung parenchyma

- Overall chest wall compliance decreases by one-third from age 30 to 75
- Intercostal muscle contraction accounts for less chest expansion in older individuals, with a relatively greater contribution from abdominal muscles

- Abdominal muscles are only partially effective in ventilating in the seated (or supine) position
- Full airway expansion occurs only in the standing position in older adults
- The diaphragm flattens and becomes less efficient
- The diaphragmatic changes likely contribute to the increase in the work of breathing during exercise, which can increase 30 percent

- With advancing age, functional reserves decrease
- In nonsmoking men,
  - forced vital capacity (FVC) decreases between 0.15 and 0.3 liters per decade
  - forced expiratory volume in 1 second (FEV1) decreases by 0.2 to 0.3 liters per decade, with steeper decline in the seventh and eight decades
- Age-related changes in women decline less steeply

- The decrease in FEV1 is accelerated after menopause
- Older persons have decreased responses to
  - Hypoxemia
  - Hypercapnia
  - Mechanical loading, such as breathing through a small-diameter endotracheal tube

- Cough is less vigorous in the older person because of
  - The age effects on respiratory muscle strength
- Mucociliary clearance is slower and less effective
- Recovery of mucociliary clearance after insult (typically viral infection) is slowed with age

GENITOURINARY SYSTEM

- Bladder
  - The prevalence of urinary incontinence increases with age
  - Until age 80, incontinence is more common in women than men, but the prevalence differences by sex subside after age 80

- Urinary incontinence is related to
  - Detrusor muscle contractility ⬇
  - Maximum bladder capacity ⬇
  - Maximum flow rate ⬇
  - Ability to withhold voiding ⬇
  - Postvoid residual (PVR) ⬆

- These functional changes are due
  - In part to decreased innervation of the detrusor muscle
  - In part to changes in the brain
- Withdrawal of estrogen in women results in
  - Decline in urethral length
  - Decreased maximal urethral closure pressure
- The urethra becomes a less effective barrier from bacterial contamination with age, especially in women

- Male reproductive system
  - A gradual decline in male reproductive ability occurs with age
  - Germ cells are formed continually, but sperm production decreases
  - The sperm from older testes
    - Increased frequency of chromosomal abnormalities
    - Impaired motility
    - Decreased ability to fertilize even when administered by intrauterine artificial insemination

- The seminiferous tubules degenerate and Leydig cell number decreases
- Changes in the epididymis and seminal vesicles are characterized by
  - Deposition of pigmented granules in the epithelial walls and amyloid in the seminal vesicle wall, which may be associated with amyloid deposition elsewhere in the body
- Enlargement of the prostate gland occurs with age

- Female reproductive system
  - The ovary ages with a decline in oocyte numbers as women enter their late fourth decade, and menopause ensues at an average age of 51 years
  - Subcutaneous fat in the pelvis is lost
  - Vaginal dryness and atrophy are
    - Mostly estrogen-dependent
    - May be compounded by age-related diminished blood flow to the vagina

MUSCULOSKELETAL SYSTEM

- Muscle
  - Muscle mass decreases in relation to body weight by about 30 to 50 percent in adults
    - The loss is not linear, but it accelerates with increasing age

- Sarcopenia, age-related loss of muscle mass and strength, is defined as
  - A decrease in appendicular muscle mass two standard deviations below the mean for young healthy adults
- Sarcopenia is an **independent** risk factor for mortality in longitudinal studies and is found in as many as 50 percent of those over 80, depending upon the population assessed

- Muscle quality decreases with infiltration of fat and connective tissue into the old muscle
- The presence of intramuscular and intermuscular fat has been termed “myosteatosis”
- Myosteatosis at the thigh has been associated with
  - Decreased strength, slower gait speed, and decreased survival in the AGES- Reykjavik study;
  - A mortality relationship was not seen with the calf myosteatosis
- The loss of muscle mass is not uniform; the loss from the legs is greater than from the arms

- Type I slow-twitch fibers are less affected by age than fast-twitch fibers
- In any muscle bundle, the size of the myofibrils decreases, followed by the number of myofibrils
- Innervation of skeletal muscle decreases in men over 50
- the number of motor units in any given muscle decreases with a compensatory increase in motor unit size
- While this synaptic remodeling occurs at all ages, the "new" neuromuscular innervations are unstable

- Some have implicated motor neuron changes as the primary cause of sarcopenia

- The loss of muscle contributes to
  - Age-related insulin resistance
  - Age-related changes in body composition
  - Volumes of distribution for water soluble drugs

- The presence of atrophied or partially or completely denervated muscle fibers can be seen on cross-section examination of muscle from an older person

- Strength also decreases dramatically with age, partially explained by loss in muscle mass

- From age 30 to age 80, a typical person's grip strength decreases 60 percent; however, activity plays an important mitigating role
- Lower-extremity strength is lost at a faster rate than upper-extremity strength
  - Activity may decrease the rate of decline but will not completely prevent it
- The net result is that strength loss is greater than muscle mass loss, with strength loss being a better predictor of disability and mortality
- The older muscle is more easily fatigued

- The recovery of older muscle after injury
  - Slowed
  - Frequently incomplete, perhaps related to a defect in satellite cells' ability to repopulate muscle
- This satellite cell defect is equally apparent in trained and sedentary older people
- Myostatin is increased, which has a potent effect to decrease muscle protein synthesis

- Bone
  - Aging increases the probability of fracture and the rate of repair is slowed, once fracture occurs
  - The increased proinflammatory environment in healthy older adults promotes bone loss
  - Anatomically, the weightbearing cortical bones lose substance from the endosteal surface
  - CT or MRI indicate that the marrow lumen of the femur is larger, the cortex thins, and fat fills much of the marrow cavities

- The aging loss of mineral occurs in both cortical (peripheral skeleton) and trabecular (axial skeleton) bone
- Trabecular number decreases and the distance between trabeculae increases with age in healthy aging women
- There is a progressive decline in osteoblast number and activity, but osteoclasts remain unchanged with age

- Precursor cells for osteoblasts remain constant in number after age 30, but their function declines, with an enhanced tendency to become adipocytes rather than bone forming
- The decline in bone mass is approximately 0.5 percent per year in healthy older people
- Age-related changes in women are compounded by menopausal changes in bone mass and function

- Vitamin D deficiency, common in older people, further accelerates bone loss

- Weightbearing exercise is
  - Frequently reduced in older adults
  - Contributing to a negative calcium balance and loss of bone mineral
- Increasing weightbearing time or increasing loading forces may increase bone mineral and prevent age-related bone loss

- Once bones fracture, the repair mechanisms are impaired in aging
- Cells isolated from old bones are less responsive to vitamin D than young ones
- The matrix in old individuals may stimulate less bone formation than that of younger people
  - This suggests that growth factors (eg, IGF-1) may be deficient or inhibitory factors may be present in the old matrix

CENTRAL NERVOUS SYSTEM

- Anatomical and physiological changes
  - The volume of the brain decreases about 7 cm3 per year after age 65, with greatest loss in the frontal and temporal lobes, greater loss of white matter than grey matter in cognitively normal older adults
  - Age-related neuronal loss is most prominent in the largest neurons in the cerebellum and cerebral cortex
  - The hypothalamus, the pons, and the medulla have modest if any neuron or volume losses with normal aging.

- Age-related neuron dropout is likely due to apoptosis (ie, programmed cell death) rather than inflammation, ischemia, or another mechanism

- Age also affects neurons that persist, with loss of the dendritic tree, shrinkage of processes, and decrease of synapses

- Neurofibrillary tangles and senile plaques occur in certain areas of the brain in normal aging but to a lesser extent than in Alzheimer disease

- More than 50 percent of cognitively normal individuals over age 85 have sufficient plaques/tangle burden to make a pathologic diagnosis of Alzheimer disease

- Acetylcholine availability decreases due to decrease in cholinergic and muscarinic neurons, and reduced release and synthesis of acetylcholine

- Dopamine and corresponding receptors in the striatum and substantia nigra may be decreased in normal aging

SKIN

- The normal aging of the skin leads to
  - Atrophy
  - Decreased elasticity
  - Impaired metabolic and reparative responses
- The epidermis becomes thinner, and the dermoepidermal junction flattens, resulting in increased fragility of the skin to shear stress
- Removing an adhesive dressing from an older person may dislodge the epidermis because the dermoepidermal junction is weaker than the bond between the skin and the dressing

- Bleeding into the space between the dermis and epidermis occurs more frequently
- Loss of undulations at the dermoepidermal junction decreases the area available for nutrient transfer, including protective lipids in the stratum corneum
- This results in dry skin (xerosis) and a compromise in the barrier function of the skin

- Epidermal turnover is slowed due to decreased division of keratinocytes and longer migration from the basal layer to the skin surface
- The epidermal cellular composition changes,
  - Decreases in melanocytes, immunologically active Langerhans cells
  - 50 percent overall reduction in nail growth and
  - Reductions in sweat and sebaceous gland activity

- The dermis
  - Thins with decrease in vascularity and in the biosynthetic capacity of the resident fibroblasts,
  - These changes contribute to delayed wound healing
- The amount of dermal collagen may be decreased by 75 percent with age, and the remaining collagen is fragmented and disarrayed
- The elastic fiber network degenerates as elastin biosynthesis declines significantly after the fourth decade

- Changes in the glycosaminoglycan macromolecules in the dermis lead to loss of hydration and decreased skin resilience
- The ability to deliver heat to the skin for excretion is impaired, especially during exercise
- With the loss of rete pegs at the dermoepidermal junction and loss of dermal capillarity, the area for heat transfer to the epidermis is decreased

- Loss of subdermal fat decreases insulation and the ability of older people to conserve heat
- Impaired thermoregulation with age
  - Tonic vasoconstriction in many older adults
  - Decreases in the amount of sweat produced by sweat glands
  - Higher core temperature before sweat

- Sensory perception of the skin decreases, particularly in the lower extremities
- Decreased sensation
  - Touch, due to decreased Meissner's corpuscles
  - Low-frequency vibration, mediated by the Pacinian corpuscles
- The skin plays a critical role in vitamin D synthesis. Ultraviolet rays convert 7-dehydrocholesterol to pre-vitamin D3 in the epidermis

- Levels of 7-dehydrocholesterol decreased with age, thus decreasing the older person's capacity for vitamin D synthesis
- Senescent cells accumulate in the skin of older people
- The microbiome of the skin changes with age such that increased diversity is seen on the older skin
- There is a decrease in subdermal fat
  - the skin wrinkling and sagging
  - increased susceptibility to trauma

SENSORY SYSTEM

- Eye
  - The structure of the eye changes with age
  - Periorbital tissues atrophy
  - eyelids become more relaxed
  - Lacrimal gland function, tear production, and goblet cell function all decrease
  - Even though tear production decreases, watering eyes becomes more common because tissue atrophy leads to displacement of the lacrimal punctum and less effective drainage

- The conjunctiva atrophies and yellows
- Deposition of cholesterol esters, cholesterol, and neutral fat in the cornea causes arcus senilis, an annular yellow-white deposit on the peripheral cornea
- The lens yellows, in part because of photo-oxidation in lens protein and an accumulation of insoluble protein

- Separation between the liquid and solid components of the vitreous may be due to collagen changes and manifest as flashes of light
- The retina becomes thinner because of a loss of neurons
- The rate of synthesis of photopigment slows with age, adding to slowed adaptation to lower light conditions
- The retinal pigment epithelium (RPE) thickens with age

- Hearing
  - With age, the walls of the external auditory canal thin
  - The cerumen becomes drier and more tenacious, increasing the risk of cerumen impaction in older people
  - The ossicular joints degenerate with age
  - Hair cells in the organ of Corti are lost, initially affecting those in the basal end of the cochlea that respond to the highest frequencie

- Neurons innervating the cochlear and in the auditory centers of the brain are lost
- The basilar membrane underlying the sensory apparatus stiffens and may calcify
- The capillaries of the stria vascularis (the source of endolymph) thicken
- The spiral ligament degenerates

- Taste and smell
  - There are visible changes in the taste buds with age, though they have modest impact on the sense
  - Although the number of papillae on the tongue decreases with aging, neurophysiologic responses of individual papillae are minimally altered, and there is no relation between gustatory acuity and number of taste buds

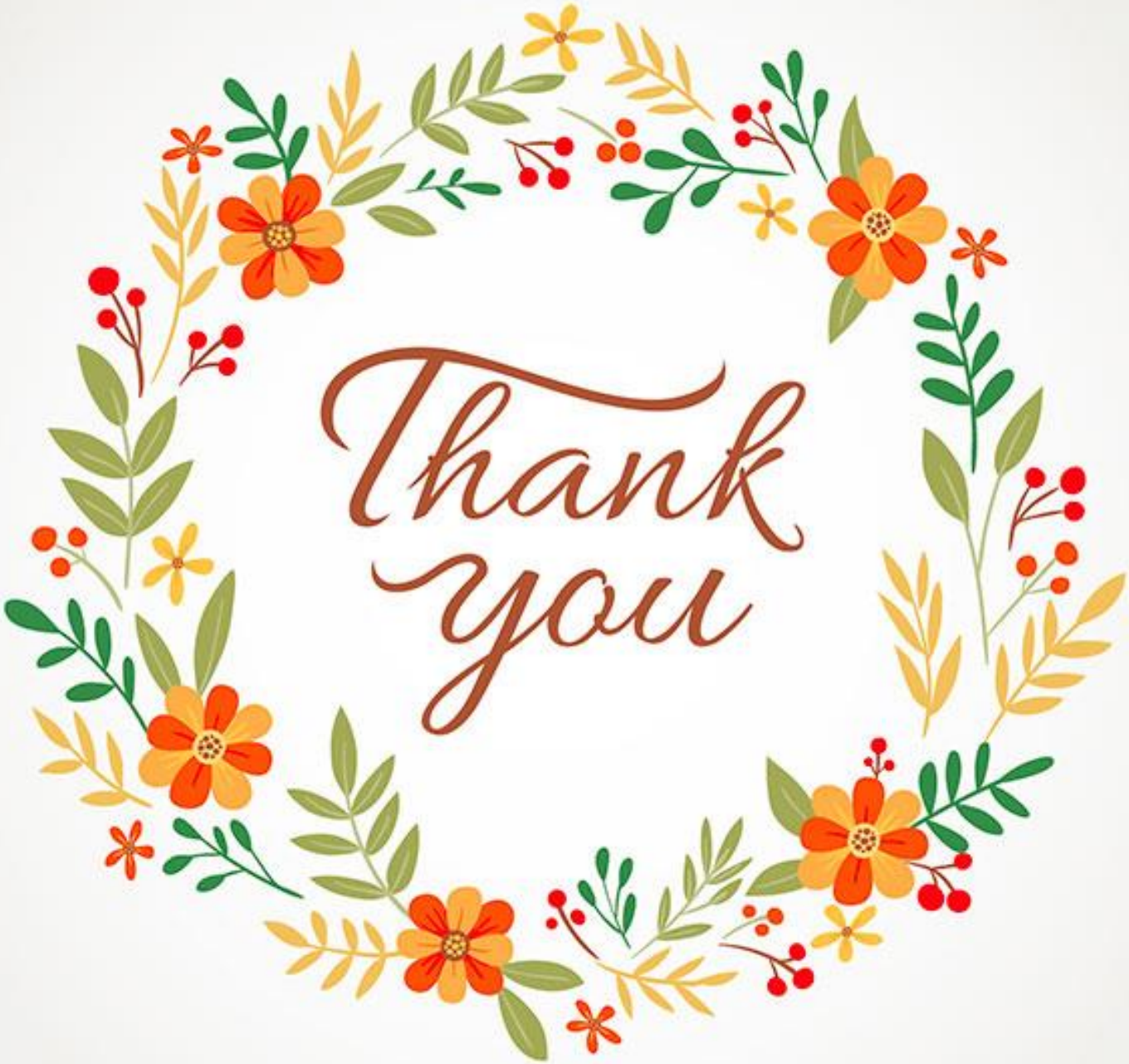
- The effects of age on the tongue need not be uniform, with regions of deficient gustatory sense becoming more common with age

- The cause of the decreased olfactory sense is unclear, but
  - The sensation area decreases
  - The number of sensing neurons decreases
  - The ability of the older person to replenish dying olfactory receptor neurons is compromised

IMMUNE SYSTEM

- General decline in the total bone marrow hematopoietic tissue with aging
- The sequential loss and shortening of telomeric DNA with advancing age lead to an increase in apoptosis (noninflammatory, programmed cell death)
- Production of pro-B cells is significantly decreased with aging, resulting in a smaller number of B cells leaving the bone marrow, while T cell precursors seem to be less affected

- Age-related changes do not affect erythroid and myeloid progenitors, and enhanced myelopoiesis is observed
- Although some innate immune mechanisms are decreased, other mechanisms appear to be more active in older individuals
  - The result of these changes is a propensity to develop chronic inflammatory states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