

Biology and Pathophysiology of Aging

Niharika Suchak, MBBS, MHS, FACP, AGSF

Associate Professor, Dept. of Geriatrics

Florida State University College of Medicine

February 23, 2018

(With special thanks to Paul Katz, MD)



Learning Objectives for Pharmacists

Upon completion of this program the pharmacist will be able to:

1. Recognize the spectrum of aging from healthy aging to frailty.
2. Describe the biology of aging and discuss common theories of aging.
3. Discuss the physiologic changes of aging and how they impact the pharmacokinetic, pharmacodynamics, and therapeutic use of medications.
4. Recognize more commonly seen atypical presentations of illness in older adults.

Learning Objectives for Technicians

Upon completion of this program the pharmacist will be able to:

1. Recognize the spectrum of aging from healthy aging to frailty.
2. Describe the biology of aging and discuss common theories of aging.
3. Recognize more commonly seen atypical presentations of illness in older adults.

Disclosure Statement

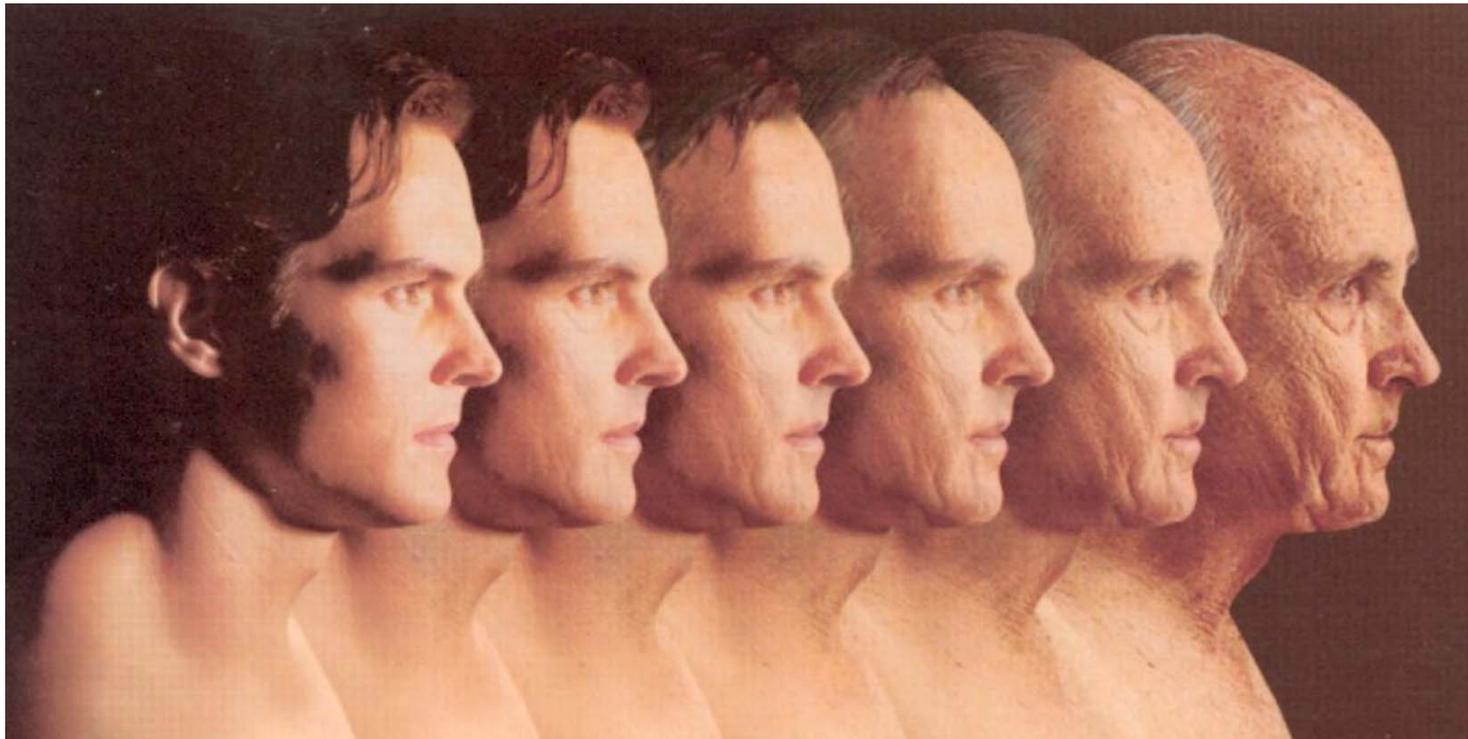
I, do not have a vested interest in or affiliation with any corporate organization offering financial support or grant money for this continuing education program, or any affiliation with an organization whose philosophy could potentially bias my presentation.

Learning Objectives

Upon completion of this program the pharmacist will be able to:

- 1. Recognize the spectrum of aging from healthy aging to frailty.**
2. Describe the biology of aging and discuss common theories of aging.
3. Discuss the physiologic changes of aging and how they impact the pharmacokinetic, pharmacodynamics, and therapeutic use of medications.
4. Recognize more commonly seen atypical presentations of illness in older adults.

We all know what aging looks like.....



<https://internetmedicine.com/aging-and-nanomedicine/>

Definition of Aging

Aging can be defined as the time-related deterioration of the physiological functions necessary for survival and fertility.

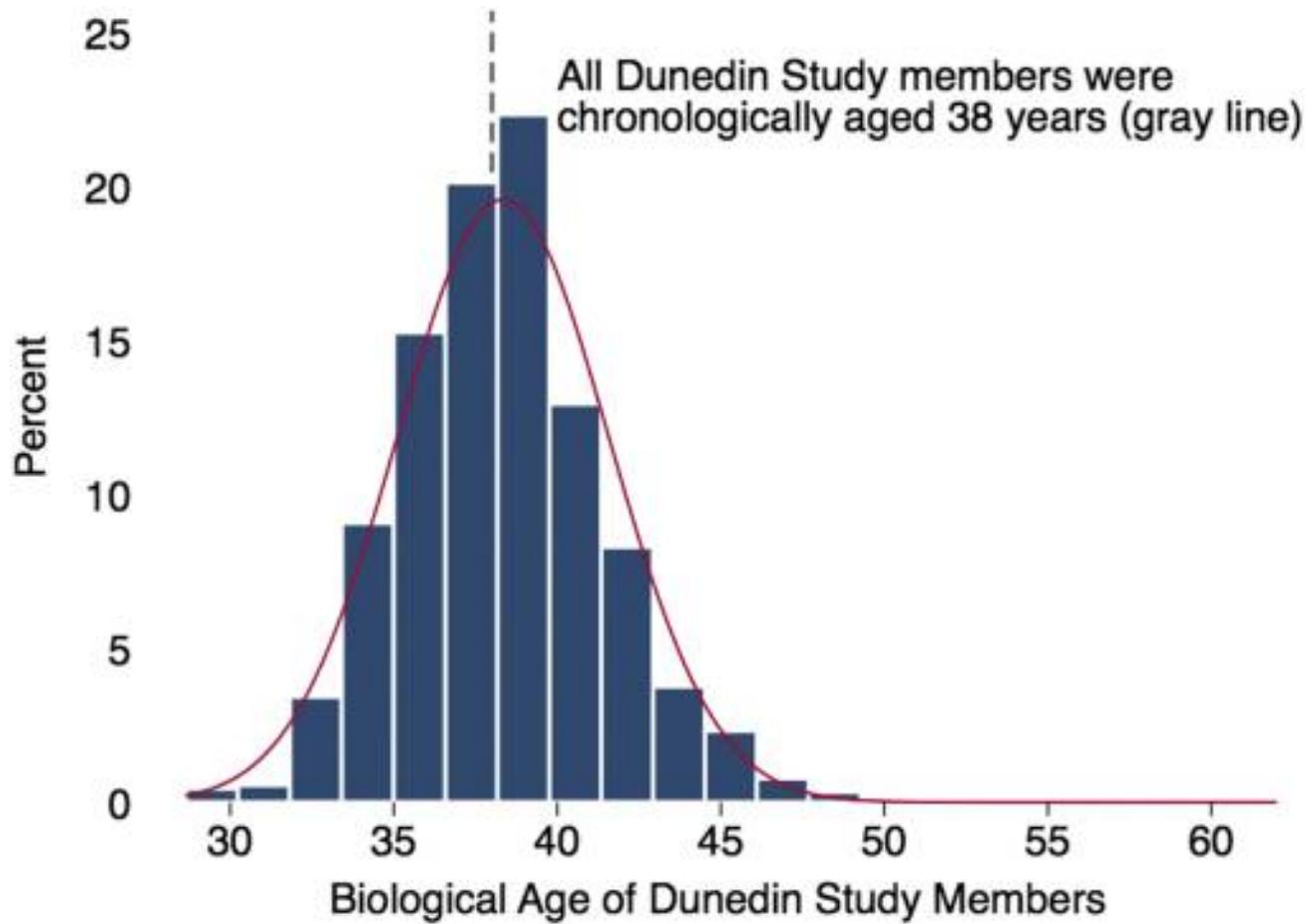
The characteristics of aging—as distinguished from diseases of aging (such as cancer and heart disease)—affect all the individuals of a species.

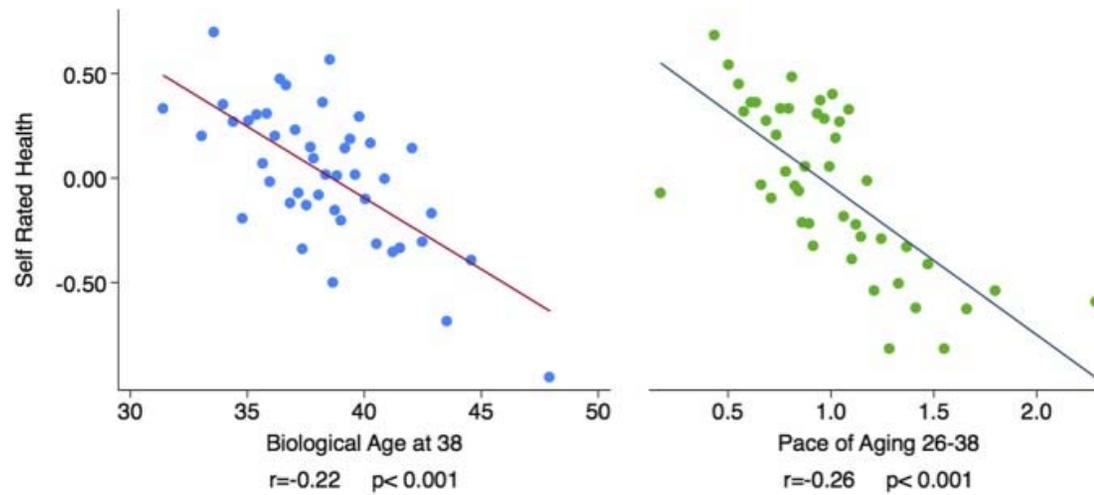
Quantification of biological aging

- 1,037 individuals followed from birth to age 38 (Dunedin study) with 95% retention rate.
- Subjects were examined at age 38 to test whether this young population would show evidence of individual variation in aging despite remaining free of age related disease.
- A 10-biomarker algorithm from the US National Health and Nutrition Survey used to measure biological age.

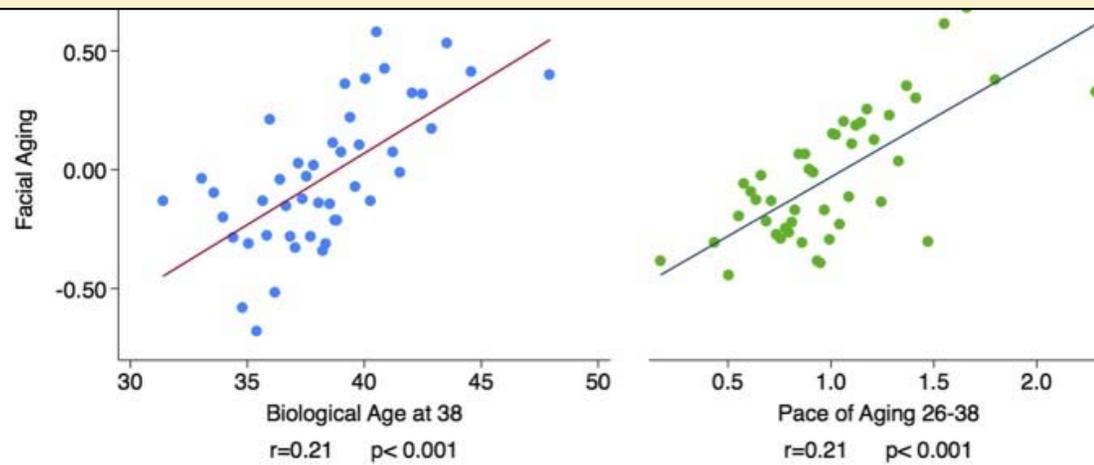
Physiologic and Metabolic Biomarkers

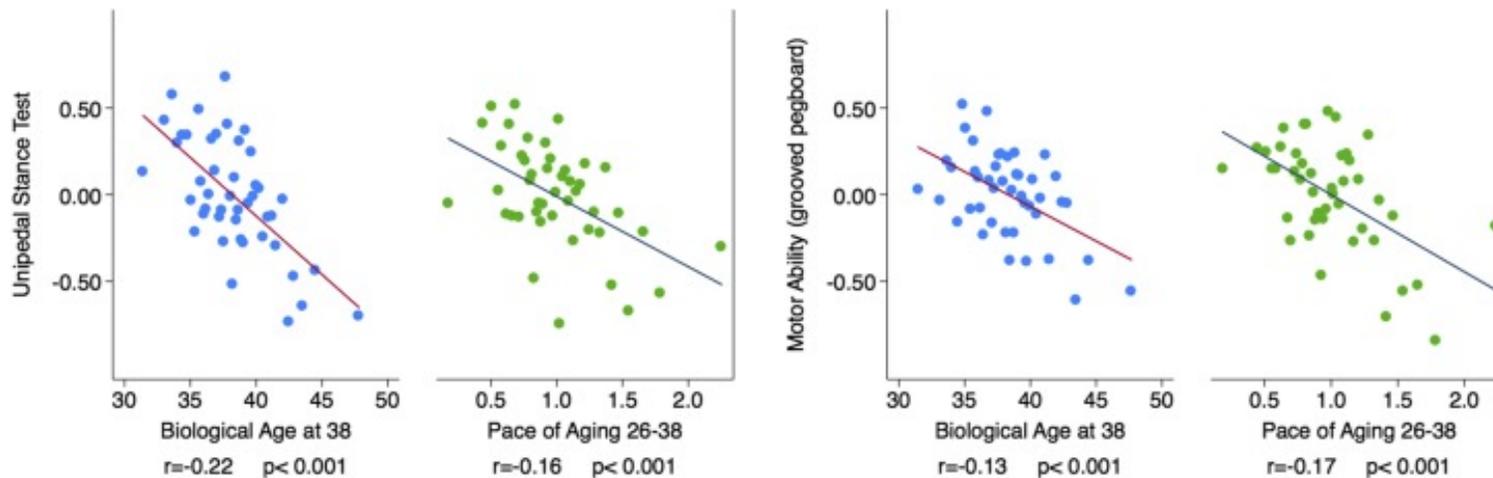
- C-reactive protein
- glycated hemoglobin
- serum albumin
- cytomegalovirus optical density (\approx IgG titer)
- serum alkaline phosphatase
- systolic blood pressure
- forced expiratory volume
- total cholesterol
- serum urea nitrogen
- serum creatinine,



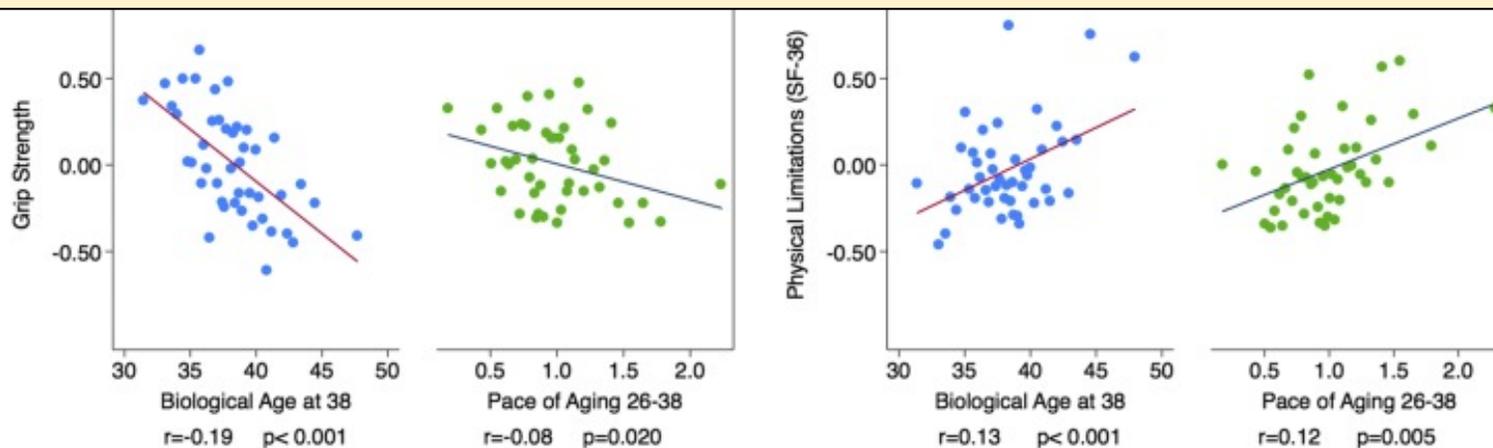


Healthy adults who were aging faster felt less healthy and were rated as looking older by independent observers.





Healthy adults who were aging faster exhibited deficits in physical functioning relative to slower-aging peers.



What is Healthy Aging?

- WHO defines *Healthy Aging* “as the process of developing and maintaining the **functional ability** that enables **wellbeing** in older age”.
- **Functional ability** is about having the capabilities that enable all people to be and do what they have reason to value. This includes a person’s ability to:
 - meet their basic needs;
 - to learn, grow and make decisions;
 - to be mobile;
 - to build and maintain relationships; and
 - to contribute to society.

<http://www.who.int/ageing/healthy-ageing/en/>

Functional ability

- Definition: Intrinsic capacity of the individual, relevant environmental characteristics and the **interaction** between them;
- **Intrinsic capacity of the person**
 - mental and physical capacities (e.g., ability to walk, think, see, hear, remember, etc.)
 - influenced by various factors (e.g., diseases, injuries, age-related changes, etc.).
- **Environments**
 - home, community, broader society;
 - all factors within them (e.g., the built environment, people, relationships, attitudes, values, health and social policies, systems that support them, services that are implemented, etc.)

<http://www.who.int/ageing/healthy-ageing/en/>

Key considerations of Healthy Aging

Diversity:

- no typical older person
- Policy should be framed to improve the functional ability of all older people, whether they are robust, care dependent or in between

Inequity:

- diversity in capacity and circumstance is the result of the cumulative impact of advantage and disadvantage across people's lives

<http://www.who.int/ageing/healthy-ageing/en/>

Frailty

- a syndrome of physiological decline in late life, characterized by marked vulnerability to adverse health outcomes
- increased vulnerability contributes to increased risk for multiple adverse outcomes
- old age itself does not define frailty
- multiple frailty screening tools: to identify older adults at high risk of adverse outcomes in a variety of clinical settings.

Frailty: epidemiology

- prevalence of frailty varies with the tool used to define frailty and with the population studied
- United States:
 - 4 to 16% in men and women \geq 65 years
 - 43 % of older patients with cancer
 - 28 – 44% prevalence of Pre-frailty
(patients at risk for frailty who fulfill some, not but all, criteria for frailty)

Factors associated with an increased prevalence of frailty:

- Older age
- Lower educational level
- Current smoker
- Current use of postmenopausal hormone therapy
- In a United States sample, African-American or Hispanic ethnicity
- Not married
- Depression, or use of antidepressants
- Intellectual disability

Frailty: screening tools

- Frailty exists on a spectrum. The end stage of the continuum of frailty is often considered to be failure to thrive.
- Physical or phenotypic frailty: multisystem biological decline leading to specific symptoms such as weight loss, weakness, and walking speed.
- Deficit accumulation or index frailty: combination of comorbidities, social situations, and disabilities (rather than a specific biology per se) that are summed to assess risk.

(Fried LP, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001; 56:M146)

[Rockwood K, Mitnitski A. Frailty in relation to the accumulation of deficits. J Gerontol A Biol Sci Med Sci. 2007 Jul;62(7):722-7.]

Physical Frailty Phenotype (Fried or Hopkins)

- **Five criteria:**

- Weight loss (≥ 5 percent of body weight in last year)
- Exhaustion (positive response to questions regarding effort required for activity)
- Weakness (decreased grip strength)
- Slow walking speed (gait speed: >6 to 7 seconds to walk 15 feet)
- Decreased physical activity (Kcals spent per week: males expending <383 Kcals and females <270 Kcal)

- **Categories:**

- Frailty: ≥ 3 criteria
- Pre-frailty: 1-2 criteria
- Not frail: none

(Fried LP, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001; 56:M146)

FRAIL scale

F atigue		Yes = 1
R esistance (ability to climb one flight of stairs)	No = 1	
A mbulation (ability to walk one block)	No = 1	
I llnesses (> five illnesses)		Yes = 1
L oss of weight (> 5% within past 6 months)	Yes = 1	

Category Score

Frailty: 3-5

Pre-frailty: 1-2

Robust: 0

(Morley JE et al. Frailty Consensus: A Call to Action. J Am Med Dir Assoc. 2013 June; 14(6): 392-397)

FRAIL-NH Scale: Frailty in the Nursing Home

SCORE (Range: 0-14) (Frailty: >7)	0	1	2
F = Fatigue	No	Yes	PHQ-9 \geq 10
R = Resistance	Independent transfer	Set up	Physical help
A = Ambulation	Independent	Assistive device	Not able
I = Incontinence	None	Bladder	Bowel
OR			
I = Illness, # of medications:	< 5	5-9	\geq 10
L = Loss of weight	None	5% in 3 months	10% in 6 months
N = Nutritional approach	Regular diet	Mechanically altered diet	Feeding tube
H = Help with dressing	Independent	Set up	Physical help

[Kaehr, Ellen et al. Frailty in Nursing Homes: The FRAIL-NH Scale. JAMDA 16 (2015) 87-89.]

	FRAIL	Potential Interventions	FRAIL-NH
F	Fatigue	Check for hypothyroidism, hypoadrenalism, Vit. B12 deficiency, sleep apnea, overtreatment with a variety of medications, Depression;	Fatigue
R	Resistance	Sarcopenia interventions:	Resistance
A	Ambulation	Sarcopenia interventions: 25(OH) Vit. D supplementation, high-quality protein intake, aerobic and resistance exercise;	Ambulation
I	Illness	Medication review for Polypharmacy and Inappropriate drug prescribing:	Illness OR Incontinence
L	Loss of wt.	Improve meal time ambience, provide adequate dietary and fluid intake, adequate time for staff to feed persons at risk, oral health, denture use	Loss of wt.
N			Nutritional approach
H			Help with dressing

[Kaehr, Ellen et al. Frailty in Nursing Homes: The FRAIL-NH Scale. JAMDA 16 (2015) 87-89.]

Physical Frailty

- Definition: “a medical syndrome with multiple causes and contributors that is characterized by diminished strength, endurance, and reduced physiologic function that increases an individual’s vulnerability for developing increased dependency and/or death.”
- Can potentially be prevented/ treated: exercise, protein-calorie supplementation, Vit D, and reduction of polypharmacy.
- Simple, rapid screening tests allow clinicians to objectively recognize frail persons, e.g. FRAIL scale.
- All persons > 70 years and all individuals with significant weight loss ($\geq 5\%$) due to chronic disease should be screened for frailty.

Interventions for Frailty management

- Exercise (resistance and aerobic)
- Caloric and protein support
- Vitamin D
- Reduction of polypharmacy

(Morley JE et al. Frailty Consensus: A Call to Action. J Am Med Dir Assoc. 2013 June; 14(6): 392-397)

Learning Objectives

Upon completion of this program the pharmacist will be able to:

1. Recognize the spectrum of aging from healthy aging to frailty.
- 2. Describe the biology of aging and discuss common theories of aging.**
3. Discuss the physiologic changes of aging and how they impact the pharmacokinetic, pharmacodynamics, and therapeutic use of medications.
4. Recognize more commonly seen atypical presentations of illness in older adults.

Theories Of Aging

- **Evolutionary theories of aging** explain historical and evolutionary aspects, addressing “why” aging exists in living things and “how” it may have evolved as a process.
- **Physiologic theories of aging** explain structural and functional age changes and elaborate a framework for translating the “what” and “where” of aging from molecules to organ systems and homeostasis.

Evolutionary Theories of Aging

- Evolution deals with the impact of natural selection (selective pressure) on the reproductive fitness of a species. An adaptive trait is one in which selection of a mutation improves reproductive fitness, whereas a nonadaptive trait is one in which there is no effect on reproductive fitness and minimal natural selection.
- There are currently two main evolutionary theories of aging: mutation accumulation theory and antagonistic pleiotropy theory.

Mutation accumulation theory

From the evolutionary perspective, aging is an inevitable result of the declining force of natural selection with age. For example, a mutant gene that kills young children will be strongly selected against (will not be passed to the next generation) while a lethal mutation with effects confined to people over the age of 80 will experience no selection because people with this mutation will have already passed it to their offspring by that age. Over successive generations, late-acting deleterious mutations will accumulate, leading to an increase in mortality rates late in life.

Antagonistic Pleiotropy Theory

A single gene is described as pleiotropic if it controls or influences multiple traits. The antagonistic pleiotropic theory considers aging an adaptive trait. Genes that can influence several traits are selected for and affect individual fitness in opposite (i.e., antagonistic) ways at different stages of life. Pleiotropic genes that have beneficial effects on early fitness components in the young but harmful effects on late fitness components are favored by natural selection. For example, there are inverse relationships between fertility and life span or between longevity and metabolic rate.

Mutation accumulation vs. Antagonistic Pleiotropy

- Note that these two theories of aging are not mutually exclusive, and both evolutionary mechanisms may operate at the same time.
- The main difference between the two theories is that in the mutation accumulation theory, genes with negative effects at old age accumulate passively from one generation to the next while in the antagonistic pleiotropy theory, these genes are actively kept in the gene pool by selection.

Physiologic Theories of Aging

- Physiologic theories address how we age.
- Over the past several decades, numerous physiologic theories have been proposed.

DNA integrity and stability

- **Target Theory of Genetic Damage:** Cumulative nuclear DNA deletions, mutations, and translocations contribute to altered functional capacity of proteins and cells.
- **Mitochondrial DNA Damage Theory:** Mutations to mitochondrial DNA occur at higher frequency than to nuclear DNA, altering efficiency of respiration/ATP production and generating more free radicals.

DNA integrity and stability

- **Telomere:** Telomere length and telomerase activity act as clock-and-winding mechanism for continued replication. Senescence is induced by loss of telomerase activity and critical telomere length.
- **Epigenetic:** Maintaining stable phenotype is epigenetic, dependent on DNA-protein interactions, DNA methylation, and histone acetylation. Phenotypic drift leads to altered gene expression and cellular function.

Defense against free radicals, Energy metabolism: Rate of living,

- **Free radicals:** Highly reactive oxygen-derived free radicals (generated through respiration) damage protein, lipid, and DNA, leading to altered structure and functional capacity.
- **Rate of living:** Changes in energy availability and in body size and composition act independently and in concert to modify life span.

Physiologic signaling: Endocrine Theory,

Response to pathogens, injury:

Immunologic Theory

Endocrine + Age-related changes in the kinetics and levels of secretion of hormones (e.g., growth hormone, cortisol, glucocorticoids) cause loss of functional capacity in target organ systems.

- **Immunologic, immunosenescence:** Time-acquired deficits in immune response and T-cell function predispose older adults to infections and disease. The accumulation of senescent immune cells increases production of pro-inflammatory cytokines, causing chronic molecular inflammation with systemic effects.

Synthesis fidelity: Error Catastrophe Theory

Clearance of defective components: Accumulation Theory

Physical reserves: Stem Cell Theory

- **Error catastrophe:** Cumulative errors in RNA and protein synthesis fidelity reach a critical threshold over time, accelerating loss of function.
- **Accumulation:** Abnormal proteins (cross-linked collagen, amyloid), lipids (lipofuscin), and/or organelles (mitochondria, membranes) are not removed, compromising cellular and tissue functional capacity.
- **Stem cell:** Stem cell/progenitor cell pools involved in tissue remodeling and repair (e.g., adult stem cells in bone, muscle, and brain) or in organ system maintenance (e.g., hematopoietic stem cells and the immune system) are depleted over time.

Learning Objectives

Upon completion of this program the pharmacist will be able to:

1. Recognize the spectrum of aging from healthy aging to frailty.
2. Describe the biology of aging and discuss common theories of aging.
- 3. Discuss the physiologic changes of aging and how they impact the pharmacokinetic, pharmacodynamics, and therapeutic use of medications.**
4. Recognize more commonly seen atypical presentations of illness in older adults.

Physiologic Changes of Aging

System or Structure	Changes	Consequences
Skin	<ul style="list-style-type: none"> ↓ collagen and subcutaneous fat Atrophy of sweat glands and decreased function ↓ sensory receptors and increased thresholds 	<ul style="list-style-type: none"> ↑ wrinkling ↓ elasticity ↑ dryness Pruritus ↓ sensory perceptions ↓ vitamin D production ↑ skin lesions
Hair	<ul style="list-style-type: none"> ↓ melanocytes ↓ hair follicle density 	<ul style="list-style-type: none"> Graying of body hair Uneven skin color Loss and thinning of hair
Eyes	<ul style="list-style-type: none"> ↓ orbital fat ↓ tears ↑ lipid around cornea ↓ elasticity & increased density of lens 	<ul style="list-style-type: none"> Sunken eyes Dry eyes Arcus senilis ↓ Visual Acuity, Cataract

Physiologic Changes of Aging

System or Structure	Changes	Consequences
Ears	Thickened tympanic membrane Atrophy of cochlea and organ of Corti	Conductive hearing loss Difficulty hearing higher-frequency sound
Respiratory	Atrophy of cilia ↓ elastic recoil Thickening and ↓ in number of alveoli	Reduced cough and clearing ↓ lung compliance ↓ PaO ₂ and O ₂ saturation
Heart	Thickening of ventricular walls Calcification of valves ↓ sinoatrial node pacer cells and bundle of His fiber ↓ compliance and stiffness of vessels ↑ peripheral vascular resistance ↓ baroreceptors response	Ventricular hypertrophy Murmurs Arrhythmias Slower rates in response to stress ↑ blood pressure Orthostatic hypotension

Physiologic Changes of Aging

System or Structure	Changes	Consequences
Gastrointestinal	<ul style="list-style-type: none"> ↓ dentine ↓ papillae on tongue ↓ saliva ↓ sphincter pressure ↓ gastric acid and hydrochloric acid ↓ blood flow and motility ↓ in number and size of cells 	<ul style="list-style-type: none"> Potential loss of teeth ↓ sense of taste Dry oral mucous membranes Heartburn ↓ absorption of iron, B12, and calcium Constipation ↓ drug metabolism and ability to detoxify
Genitourinary	<ul style="list-style-type: none"> ↓ renal mass, nephrons, glomerular filtration rate, blood flow ↓ smooth muscle and elastic tissue ↓ sphincter control ↓ renin, angiotensin and aldosterone 	<ul style="list-style-type: none"> ↓ ability to concentrate urine ↓ control and possible incontinence ↓ capacity ↑ frequency, urgency, and nocturia ↓ activity of RAAS: ↓BP regulation

Physiologic Changes of Aging

System or Structure	Changes	Consequences
Female Reproductive	↓ hormones and pelvic elasticity	Thin, pale vaginal mucosa
Male Reproductive	Enlarge prostate ↓ testosterone	Prostate hypertrophy Tendency of testes to hang lower
Musculoskeletal	Narrow intervertebral discs ↓ bone mass, bone growth and osteoblastic activity ↓ number of muscle fibers Muscle atrophy Stiffening of ligaments and tendons ↓ cartilage	Loss of height (1 to 4 inches) Kyphosis ↑ risk for osteoporotic fractures ↓ strength ↓ strength ↓ agility ↓ ROM and mobility

Physiologic Changes of Aging

System or Structure	Changes	Consequences
Neurological	<ul style="list-style-type: none"> ↓ brain size, weight and volume ↓ neurons, glial cells, and conduction of nerve fibers 	<ul style="list-style-type: none"> ↓ processing and reflexes Delayed reaction time ↓ psychomotor performance
Endocrine	<ul style="list-style-type: none"> ↓ basal metabolic rate ↓ sensitivity to hormones ↓ febrile response 	<ul style="list-style-type: none"> ↑ weight ↓ insulin response, glucose response, glucose intolerance and sensitivity of the renal tubules to ADH ↓ shivering and sweating
Immune/ Hematologic	<ul style="list-style-type: none"> ↑ autoantibodies ↓ memory of previous antigenic stimuli ↓ responsiveness to immunization 	<ul style="list-style-type: none"> ↓ response to acute infection ↑ incidence of malignancy

Pharmacokinetics

- Pharmacokinetics is the study of **how the body processes a specific drug** after its administration including absorption, distribution, metabolism, and elimination.
- After a drug is absorbed and distributed in the body, it is processed or metabolized (and/or detoxified) and then eliminated (or excreted) from the body.
- Every drug has a specific pharmacokinetic profile based on specific parameters such as age, sex, weight, body mass index, liver function, and kidney function.

Absorption of oral medications

- Absorption of certain medications can be affected by age associated changes in the gastrointestinal (GI) tract.
- The aging process may be associated with decreased GI motility, decreased GI blood flow, and decreased gastric acid secretion (with an elevation in gastric pH).
 - Decreased gastric blood flow and increased gastric pH may cause reduced drug absorption.
 - Decreased GI motility may result in more of the drug(s) being absorbed.

Drug Distribution

- Drug distribution refers to where the drug goes after it enters the bloodstream.
- For drugs that are administered by mouth (i.e. the oral route), the distribution phase begins after absorption.
- Various factors influence the volume of distribution of a drug, such as:
 - protein binding (only unbound drug is distributed)
 - pH
 - molecular size
 - water or fat solubility (fat-soluble drugs usually have greater volume of distribution due to increased proportion of body fat with aging)

Drug Distribution and the Aging process

- Distribution of a medication in the body can be affected by age associated changes in body composition and changes in various organ-systems.
- As the body ages, there is decline in muscle mass with an increased proportion of body fat and a reduction in total body water.

Drug Distribution and the Aging process (cont'd)

- Fat soluble drugs --- greater volume of distribution in an older adult, e.g. benzodiazepines (increased elimination half-life and prolonged effect) -- reduction in dose and/or dose interval when used in an older adult
- For drugs distributed in muscle tissue, the volume of distribution may be reduced.
- Water soluble drugs -- reduced volume of distribution in an older adult, e.g. digoxin (increased initial drug concentration) -- reduction in dose and/or dose interval when used in an older adult

Drug Distribution and the Aging process (cont'd)

- Older adults produce less albumin (albumin binds drugs in the bloodstream); with reduction in protein binding -- increase in free (unbound) drug concentration in the blood.
- Increased free (unbound) drug concentration in the blood -- more drug becomes available to reach receptors -- increases pharmacologic effect in older adults.
 - For example, phenytoin, a highly protein (albumin)-bound antiseizure medication, may have a significant effect in older adults who usually have reduced albumin levels. In such a situation, there is more free phenytoin available that can cause various adverse effects.

Drug Metabolism

- The liver is the primary organ responsible for drug metabolism or drug processing. The liver can both synthesize various proteins, substrates, and enzymes and convert chemicals from one form to another.
- The detoxification component of drug metabolism (or processing) converts substances believed to be harmful to the body to a form that can be eliminated more easily.
- In general, the final by-product of liver metabolism is a water-soluble product that is easily eliminated via the kidney.

Drug Metabolism (cont'd)

- Alteration of normal metabolic process can affect pharmacokinetics of drug.
- Metabolic process can be affected by many factors:
 - diet, genetics, alcohol, nutritional status,
 - sex, presence (or absence) of interacting drugs
- If metabolism is decelerated, half-life of the drug gets prolonged -- delay in elimination -- potential for adverse drug reactions (ADRs) increases.
- If metabolic process is hurried, half-life of the drug is reduced – drug effectiveness may be reduced because of early elimination.

Drug Metabolism and the Aging Process

- The aging process also can affect drug metabolism.
- Several physiological changes can significantly impact metabolic capacity.
 - Usually, liver blood flow is reduced in older adults, which can greatly affect metabolism because the drug is introduced to the liver at a much lower rate.
 - Liver mass and intrinsic metabolic activity also is reduced during the aging process.

Source: Wooten, JM. Pharmacotherapy Considerations in Elderly Adults. South Med J. 2012;105(8):437-445.

Effect of aging on the cytochrome P-450 system

- Cytochrome P-450 content declines incrementally with age, fourth decade onwards.
- Isozyme CYP3A4
 - involved in the metabolism of >50% of marketed medications
 - age-related reductions in drug clearance for CYP3A4 substrates
- Isozyme CYP2D6
 - involved in the metabolism of 25%–30% of marketed medications
 - minimal age-related changes
 - 10% of white people are deficient in CYP2D6 (called poor metabolizers [PMs])

Drug Elimination (or Excretion)

- Elimination of drugs from the body occurs primarily via excretion through kidneys.
- As with metabolism, the half life of drugs is increased as kidney function is reduced.
- Reduction in blood flow to the kidneys, decrease in kidney mass, and reduction in size and number of functioning nephrons contributes to age associated decline in kidney function .

Source: Wooten, JM. Pharmacotherapy Considerations in Elderly Adults. South Med J. 2012;105(8):437-

Drug Elimination (or Excretion) (cont'd)

- Unlike liver changes observed with aging, kidney changes can be anticipated, thus allowing drug dose adjustment based on kidney function that is either measured or calculated.
- Calculations based on laboratory measurements (e.g., serum creatinine) or other data can be used to estimate a patient's kidney function. Pharmaceutical manufacturers use these estimates to provide dosing

Source: Wooten, JM. Pharmacotherapy Considerations in Elderly Adults. South Med J. 2012;105(8):437-

GFR (glomerular filtration rate)

- GFR declines gradually with age, even in people without kidney disease; variation among individuals; reasons for decline not known.
- The Cockcroft and Gault (C-G) equation estimates creatinine clearance and is not adjusted for body surface area.
- The MDRD Study equation estimates GFR adjusted for body surface area. GFR estimates from the MDRD Study equation can therefore be applied to determine level of kidney function, regardless of a patient's size.

2014 National Kidney Foundation. Frequently Asked Questions About GFR Estimates.

Estimation of Kidney Function for Prescription Medication Dosage in Adults

- For most drugs tested, there was little difference in the drug dose that would be administered using either equation to estimate kidney function.
- Use of a single kidney function estimate to guide detection, evaluation, and management of chronic kidney disease (CKD) and drug dosing is likely to facilitate delivery of high-quality health care.
- <https://www.niddk.nih.gov/health-information/professionals/clinical-tools-patient-education-outreach/ckd-drug-dosing-providers>
Utilize eGFR or eCrCl for drug dosing.
- If using eGFR in very large or very small patients, multiply the reported eGFR by the estimated body

Summary: pharmacokinetic changes observed with aging

Pharmacokinetic parameter	Altered physiology with aging	Comments
Absorption	<ul style="list-style-type: none"> ↓Gastric secretion ↑Gastric pH ↓GI motility ↓GI blood flow 	<p>Many drugs may diminish in their absorptive ability; Time of onset of drug action may be delayed; Amongst the various pharmacokinetic parameters, absorption is least affected by aging;</p>
Distribution	<ul style="list-style-type: none"> ↓Total body water ↓Lean body weight ↓Albumin ↑Body fat 	<p>Increased free fraction of drug; Increased volume of distribution of lipid soluble drugs;</p>
Metabolism	<ul style="list-style-type: none"> ↓Enzyme induction ↓Liver mass ↓Liver blood flow 	<p>Reduced liver clearance of drugs; Increased potential for drug interactions;</p>
Elimination	<ul style="list-style-type: none"> ↓GFR (glomerular filtration rate) ↓Kidney blood flow 	<p>For older adults, drug accumulation will occur for drugs eliminated by kidneys;</p>

Source: Wooten, JM. Pharmacotherapy Considerations in Elderly Adults. South Med J. 2012;105(8):437-445.

Pharmacodynamics

- Pharmacodynamics is the study of **how a specific drug affects the body**.
- All drugs have specific mechanisms of action and various adverse effects that are caused by pharmacological interactions in the body.
 - The aging process may induce more or less sensitivity to particular medications.
- This is especially important for drugs that affect the cardiovascular and/or central nervous systems:
 - May be related to effects that certain drugs have on receptor sites
 - As the body ages, the affinity and number of receptor sites may change over time, which can affect the efficacy of some drugs

Pharmacodynamics and the Aging Process

- Because of the physiological aspects of aging, older adults may be at high risk for certain drug adverse effects.
- For example,
 - Anticholinergic/antihistamines frequently cause urinary retention. This may not be a problem for younger patients, but it may be a severe problem for older male patients with benign prostatic hypertrophy (BPH).
 - Patients maintained on certain blood pressure medications for many years may experience sudden precipitous drops in blood pressure caused by age induced orthostatic hypotension. These are basic adverse effects of drugs, but they are precipitated by age related physiological changes.

Learning Objectives

Upon completion of this program the pharmacist will be able to:

1. Recognize the spectrum of aging from healthy aging to frailty.
2. Describe the biology of aging and discuss common theories of aging.
3. Discuss the physiologic changes of aging and how they impact the pharmacokinetic, pharmacodynamics, and therapeutic use of medications.
- 4. Recognize more commonly seen atypical presentations of illness in older adults.**

Atypical presentations of illness

- Typical presentations of common illnesses are addressed in healthcare education.
- . “atypical” : lack the usual signs and symptoms characterizing a particular condition or diagnosis.
- Atypical presentations of illness are common in older adults.
- For example, a change in behavior or functional ability is often the only sign of a new, potentially serious illness.

Atypical presentations of illness

- The definition of an atypical presentation of illness is: *when an older adult presents with a disease state that is missing some of the traditional core features of the illness usually seen in younger patients.*
- Atypical presentations usually include one of 3 features:
 - (a) vague presentation of illness,
 - (b) altered presentation of illness, or
 - (c) nonpresentation of illness (i.e., underreporting)

Atypical presentations of illness: Risk Factors

- Increasing age (especially age 85 years or older)
- Multiple medical conditions (“multimorbidity”)
- Multiple medications (or “polypharmacy”)
- Cognitive or functional impairment

Atypical presentations of illness: Symptoms

- Change in behavior: Acute confusion (i.e., delirium), Agitation
- Anorexia (or change in appetite)
- Absence of fever
- Absence of pain, or pain in alternate location
- Generalized weakness
- Fatigue
- New urinary incontinence
- New functional decline (i.e., change in mobility)
- Fall

Atypical presentations of illness: Questions

- Is the patient usually quiet and nonconversant or is this a change?
- Have you noticed the patient to be more “fidgety” or more hyperactive?
- Has there been any weight loss?
- Are there any new medications that were started when the symptoms started?
- In the past, when patient has had an infection, what signs has the patient had?
- I see the patient is in a wheelchair, can the patient walk, or is this a new change?

Illness	Atypical Presentation
Infectious diseases	Absence of fever Sepsis without usual leukocytosis and fever Falls, decreased appetite or fluid intake Confusion Change in functional status
“Silent” acute abdomen	Absence of symptoms (silent presentation) Mild discomfort and constipation Some tachypnea and possibly vague respiratory symptoms
“Silent” malignancy	Back pain secondary to metastases from slow-growing breast masses Silent masses of the bowel
“Silent” myocardial infarction	Absence of chest pain Vague symptoms of fatigue, nausea and a decrease in functional status Classic presentation: shortness of breath - more common than chest pain

Illness	Atypical Presentation
Nondyspneic pulmonary edema	<p>May not subjectively experience the classic symptoms of paroxysmal nocturnal dyspnea or coughing</p> <p>Typical onset may be insidious with change in function, food or fluid intake, or confusion</p>
Thyroid disease	<p>Hyperthyroidism presenting as “apathetic thyrotoxicosis” (i.e., fatigue and a slowing down)</p> <p>Hypothyroidism presenting with confusion and agitation</p>
Depression	<p>Lack of sadness</p> <p>Somatic complaints: appetite changes, vague gastrointestinal symptoms, constipation, and sleep disturbances</p> <p>Hyperactivity</p> <p>Sadness misinterpreted as normal consequence of aging</p> <p>Medical problems that mask depression</p>
Medical illness that presents as depression	<p>For example, hypothyroid and hyper disease that presents as diminished energy and apathy</p>

