Physiology of Aging

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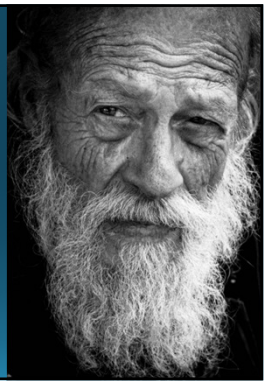
UND School of Medicine and Health Sciences



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Why should we understand normal aging ?

Distinguish age - related changes from disease in late life.

Example: what are normal cognitive changes versus early dementia in older adults?

3

Objectives

- Avoid attributing disease as normal aging
- Report biological aging and its pace
- Set appropriate diagnostic thresholds (e.g., renal dosing)
- Anticipate altered physiologic responses (e.g., orthostasis)

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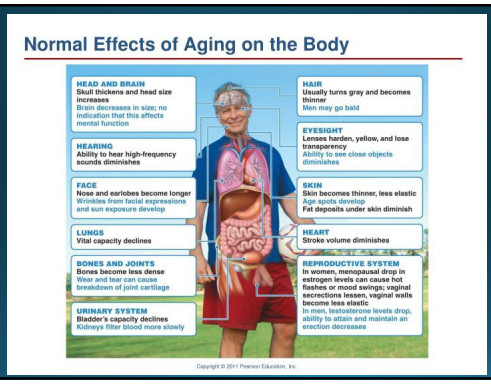

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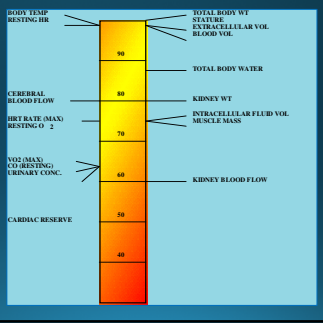
Anatomic & functional changes



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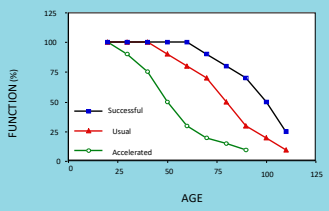
The Aging Process



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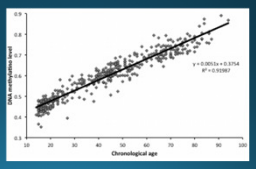
Pace of Aging

Blood / Physiologic tests
- Blood pressure
- Girth
- Lung function
- Grip strength
- Blood tests (liver, renal, immune)

Molecular Biomarkers
- DNA methylation patterns



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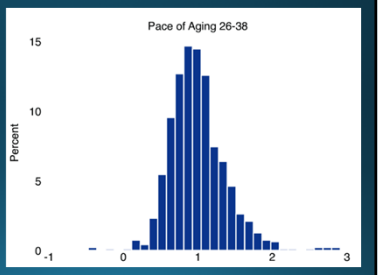
DunedinPACE

- Built from 20 years of longitudinal aging data
- **1.0 = aging at the average rate**
- **<1.0 = slower aging**
- **>1.0 = faster aging**



PNAS (2015) dio - 10.1073/pnas.1506264112

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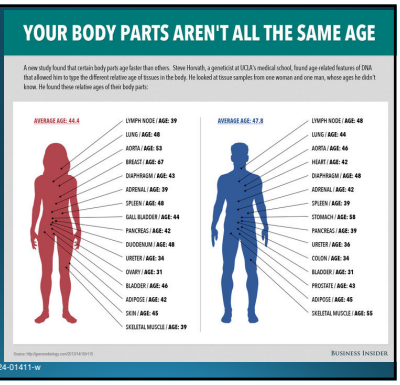
ORGAN – SPECIFIC AGING



Nat Med (2023).doi.org/10.1038/s41591-023-02296-6
GeroScience 47, 1411–1423 (2025). https://doi.org/10.1007/s11357-024-01411-w

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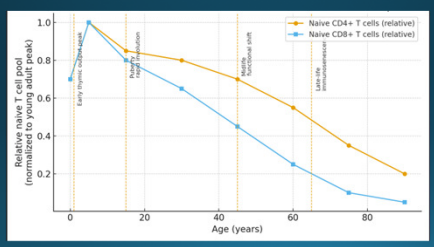
Different aging trajectories within the immune system



Nature Immunology (2025) doi 10.1038/s41590-024-02059-6

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Aging HENT

Daniel Popper

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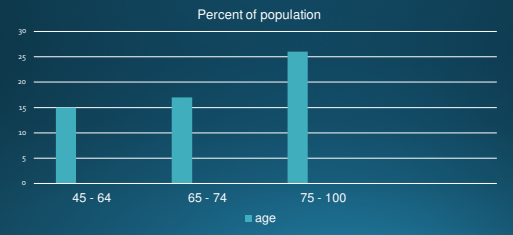
Aging Eye: vision impairment prevalence



Lighthouse National Survey on Vision Loss

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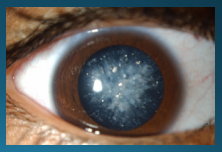
THE AGING EYE

- iris rigidity
- 2.5 mm pupil aperture decrease
- lens crystalization / opacification
- syneresis: vitreous gel contraction & separation of solid / liquid components
- retinal thinning, loss of foveal reflex



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Visual functional changes with age

- ↓Contrast sensitivity
- ↓Glare recovery
- 60% less light reaches retina (due to lens changes and pupil constriction)
- Presbyopia: inability to focus on close objects (print)
- Night vision
- Decrease peripheral vision

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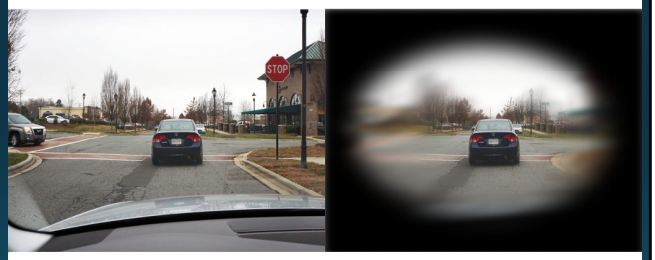
Normal Vision

Vision With Glaucoma*



*Degree of side (peripheral) vision loss varies based upon severity of disease

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SMD

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Clinical implications of age – dependent vision changes

- Driving ability (night)
- Falls
- Loss of IADLs / ADLs (transportation, finances)
- Social isolation
- Depression

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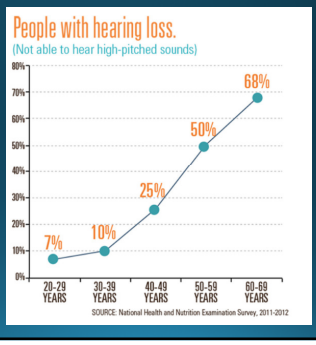

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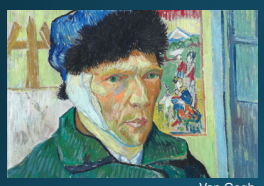
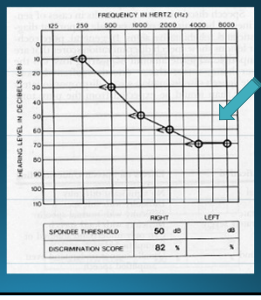
Neurosensory hearing loss



Van Gogh



10-dB loss per decade

20

PRESBYCUSIS

Bilateral high-frequency hearing loss
- Insidious, recognized when loss dips below 8000 Hz
- Tinnitus
- M > F rate of hearing loss
- r/o hypothyroidism

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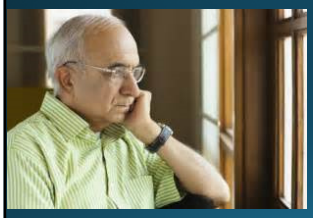
Psychosocial / functional implications of presbycusis



- deterioration in communication
- sense of isolation
- false association with senility
- depression / paranoia
- functional impairment

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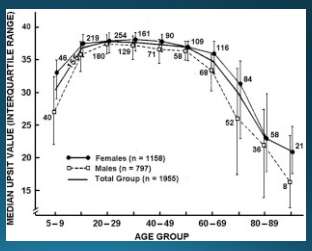
Naso – pharynx changes

- 62 % older adults 80 + have olfactory impairment
- Sense of taste declines for sour, salty and bitter. (sweet preserved)



Journals of Gerontology: Medical Sciences. 2015; 70(11):1435–1441

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Oral aging

- Salivary flow does not change (meds)
- Loss of taste buds and regional taste deficits (exacerbated by olfactory changes)
- Edentulous rates 25 %

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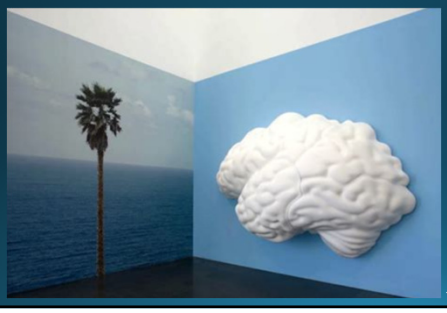
Normal Neurologic Aging



- Cortical changes
- Peripheral system
- Autonomic system

John Baldessari

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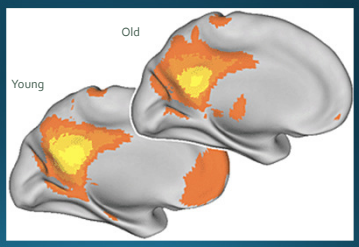
Age – dependent changes in

- Cerebral volume
- Perfusion
- Metabolism



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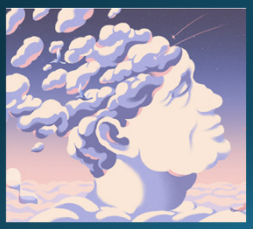
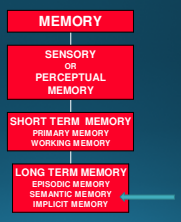
Memory changes





Not connected with event.

"Tip of the Tongue" word search

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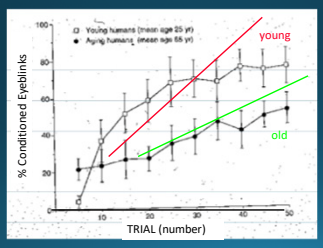
Altered Sensory-Perceptual Memory



Disterhoff, et al.

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Learning & Aging

Memorization
- Recall of mini-golf score:
- Young = Old without auditory distraction
- Young > Old with auditory distraction

Learning
- Slower learning curve
- Lower total amount learned

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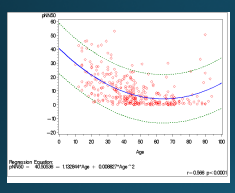
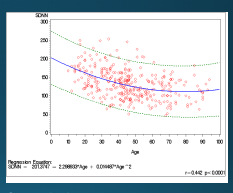
Autonomic Nervous System Changes with Age



Parasympathetic

(pNN50 = Percentage of successive normal sinus RR intervals > 50 ms)



Sympathetic

(SDNN = Standard deviation of all normal sinus RR intervals)

American Journal of Cardiology. 2010; 105(8):1181–1185.

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Heart Rate Variability in Older Adults

Study	n	time (yrs)	HRV parameter	Mortality rate
1994 Framingham	736	4	1 std deviation decline in low frequency HRV	↑ 1.7
1999 deBryne	5272	4	lowest HRV quartile	↑ 1.8
1997 Dekker	878	30	low HRV (< 20 ms)	↑ 2.1

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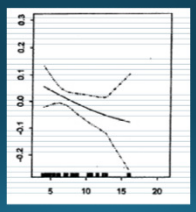
Environmental stress accentuates age-dependent decline in HRV

Heart Rate Variability



Particulate Matter (PM2.5)

J. Exp. Anal. & Envir. Epi. 11:118, 2001

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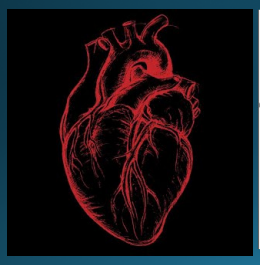
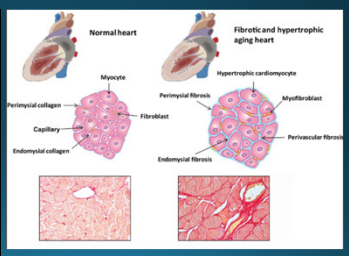
Cardiovascular changes





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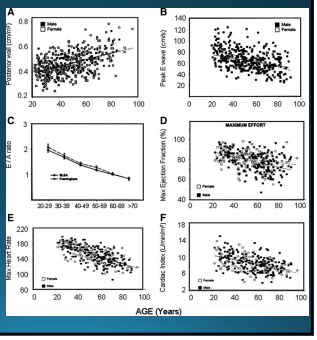
Normal Aging

- Peak HR declines (220 – age)
- Peak Cardiac Output declines
- Peak EF declines
- LV stiffens, can't relax
- Valvular regurgitation
- Prolongation PR, QRS, QT



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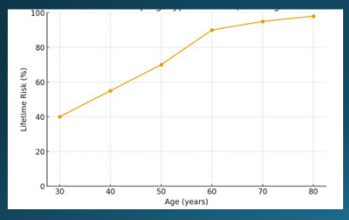
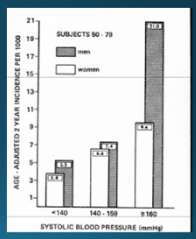
Systolic BP rises with Age



Life - time risk of hypertension



Framingham Heart Study

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Clinical implications

- Increase awareness of hypertension management
- SPRINT study = target 120 systolic for optimal outcomes,
- Looser BP control with frailty and end – of – life
- Recognize pseudo hypertension
  - Osler sign (palpable radial artery despite cuff inflation)
  - ABI > 1.3
  - Office vs home BP mismatch
  - No end organ injury

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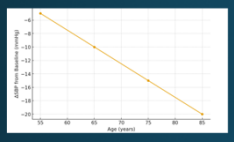
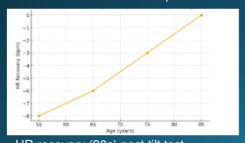
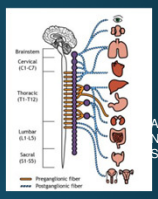
Circulatory recovery



SBP recover at 30 seconds post tilt test

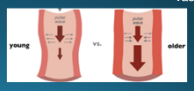


HR recovery (20s) post tilt test



Autonomic Nervous System

Vascular



Circulation (2014) DOI: 10.1161/CIRCULATIONAHA.114.009831?

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Clinical implications

Older adults after postural change

- Slower BP stabilization
- Diminished HR recovery
- Increased risk for unsteadiness, dizziness, falls and syncope

- Supine hypertensives with orthostasis have lower global cognitive scores J Gerontol (2013) DOI: 10.1093/gerona/glt171

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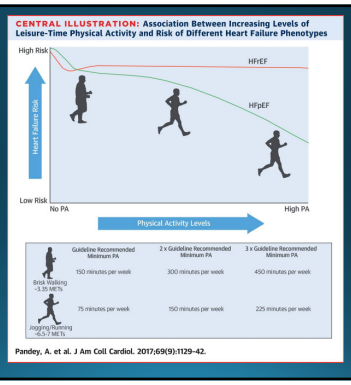
More is Better



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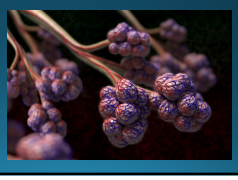
Aging respiratory system

- Senile emphysema: alveoli enlarge without destructive changes
  - Reduced surface tension
  - Lower elastic recoil
  - Increased macrophages
  - Senescent cell phenotype



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Pulmonary changes with age

Anatomic changes	Effect	Implications
Alveolar dilation	Reduced surface tension Reduced lung recoil	FEV1 declines more than FVC and overestimate COPD in age with FEV1/FVC < 0.65 Poor gas exchange
Chest wall stiffens	Decreased Compliance, FEV1	Ineffective cough reflex Infection
25% decline in diaphragmatic strength	25% less strength 30% lower mean Max Inspiratory Pressure	Increased work and fatigue with stress
V/Q inequalities	Low ventilation in lower lungs	CO2 retention
FEV1 declines	0.3 L per decade	Decreased gas exchange
TLC does not change with age (VC + RV)	Increased RV, decreased VC	More air trapping

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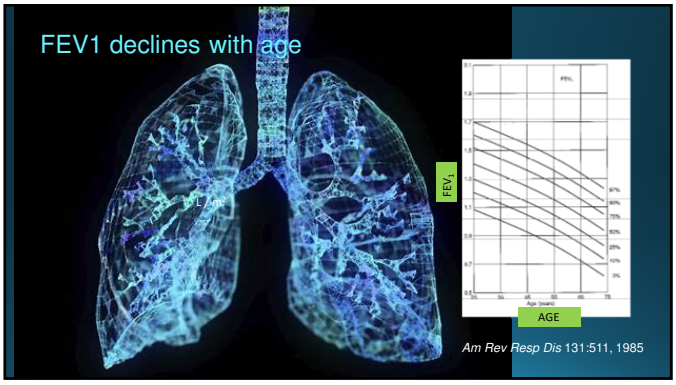
FEV1 declines with age



Am Rev Resp Dis 131:511, 1985

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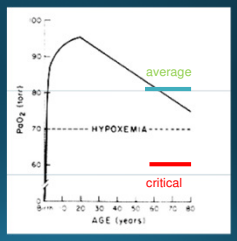
Pulmonary changes with age

- Arterial oxygen tension PaO_2 declines
- Arterial carbon dioxide PaCO2 unchanged



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Clinical implications

- Early closing volume
  - Atelectasis with hypoxia
  - Pneumonia
  - Promote up – right position

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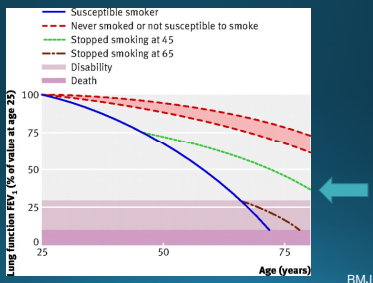
Smoking cessation reverses aging lung decline



BMJ (e – pub, March 6, 2008)

Parkes, G. et al. BMJ 2008

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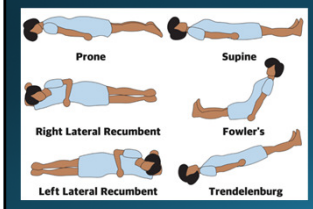
Key point !

- supine position exaggerates age-dependent decrements in pO_2 and hypoxemia



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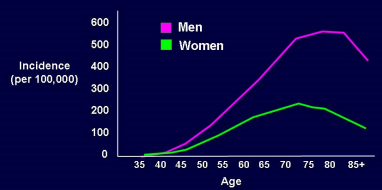
Incidence of Lung Cancer Increases With Age

U.S. incidence of lung cancer by age



Yancik R. et al. *Comprehensive Geriatric Oncology*. 1998:95–104.

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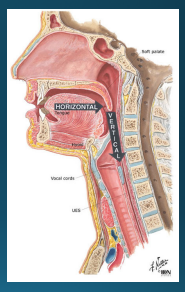
Aging GI system

Swallow problems
Xerostomia (25%)
Poor dentition
Bone loss

Silent aspiration (10%)
Reduced oral → pharynx (60%)



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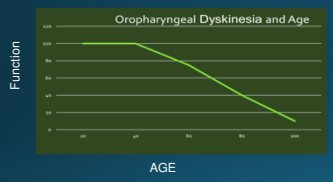
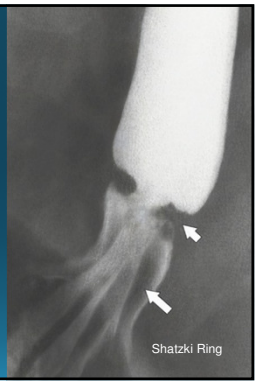
Dysphagia



Regular post prandial coughing or choking, think aspiration



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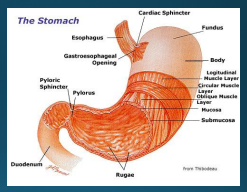
Aging GI system

Esophagus:
- reduced contractions
- Simultaneous contractions
- Rapid peristaltic wave
- Decreased acid clearance

Stomach
- decreased elasticity
- reduced antral volume
- lower resistance to mucosal injury



N. Salles. Basic Mechanisms of the Aging Gastrointestinal Tract. *Dig. Dis.* 25: 112 – 117, 2007.

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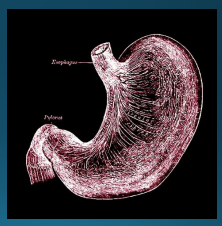
Age – dependent decline in mucosal defenses

- Normal acid secretion
- Decrease HCO_3 and mucus secretion (cytoprotection)
- NSAID damage
  Cyclo-oxygenase inhibition:
  - Lowers mucus production
  - Lowers bicarbonate secretion
  - Decreases proliferation and repair (anti-cancer)



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Clinical consequences of aging stomach

- GERD: affects 30 % elderly
  - Aspiration pneumonia
- Reduced antral volume
  - Earlier feeling of fullness
- Nutritional deficits
  - Higher protein calorie requirements
- Atrophic gastritis
- NSAID gastropathies
  - GI bleeding

Digestion 51:24-29, 1992

Gastroenterology 101: 977, 1991

Ann Int Med 109: 359, 1988
Ann Int Med 114: 259, 1991
Ann Int Med 114: 307, 1991

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Intestinal aging

- Minor changes with age in small bowel

⇩ Lactase levels
--increase lactose intolerance
--bacterial overgrowth

⇩ -- folate, iron, calcium, vit D, B12 absorption

⇧ -- pain, bloating, weight loss
-- adult FTT syndrome

Diverticulosis
Ischemic colitis
C. difficile colitis

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The dreaded fecal impaction

- Decreased mucosal secretion
- muscle layer atrophy
- abdominal wall weakness
  - Gerontology 29: 181.
  - Clin Geriatr Med 15: 499

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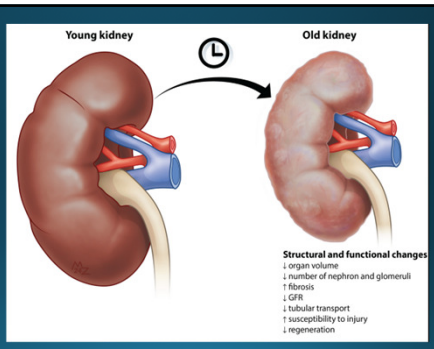
Kidney

↓ GFR (average 0.8–1 mL/min/yr after age 40)



American Journal of Physiology-Renal Physiology https://doi.org/10.1152/ajprenal.00287.2024

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Clinical implications

Reduced renal clearance
- drug toxicity risk

Blunted RAAS
- impaired response to hypotension and susceptibility to fluid overload

Axiom:
- start low and go slow with renally cleared meds

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Musculo-skeletal changes

Unconditioned versus Exercise

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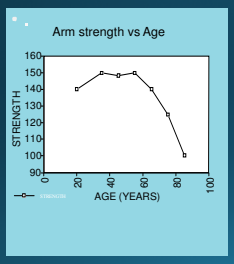
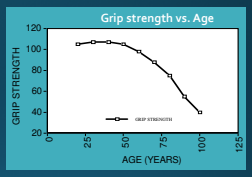
Strength changes





- Muscle mass loss 1 - 2 % annually
- Muscle strength loss 3 – 4 % annually

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Clinical implications

- Disability
- 30% women and 15% men unable to lift 10 lbs.
- 40% elderly with limits in daily tasks (e.g., transferring)
- Hospital – induced deconditioning

- Sarcopenia: muscle atrophy
- Dynopenia: age – related muscle weakness

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Physical activity prevents functional decline in 65 +

Established Population for Epidemiological Studies of Elderly

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Summary of normal aging

- Aging is not a disease
- Aging processes lead to chronic conditions
- Delay of aging will prevent chronic conditions

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