. Glomular filtration ↓ 20%
. Cardiac index ↓ 30 %
. Max breathing capacity ↓ 40 %

Drugs in elderly

- **Drug-related problems in older adults are common and cause significant morbidity.**
- **Common medical conditions in the elderly include: hypertension, diabetes mellitus, osteoporosis, bronchial asthma, COPD, cancer, arthritis, heart diseases, Alzheimer's disease and cognitive dysfunction, and stroke.** → impact therapy

- **The most common sensory impairments are difficulties in hearing and vision.** (Can't read prescription)
- **The elderly are also prone to falls.**

Clinical manifestations of normal aging include:

1. Changes in biochemical makeup of tissues.
2. Reduced functional capacity of body systems.
3. Reduced ability to adapt to physiological stress.
4. Increased vulnerability to disease.
5. Frailty (weakness, fatigue, weight loss and functional decline). (ضعف و هشاشة)

- **Individuals experience aging at different rates.**

TABLE 60–1 Some changes related to aging that affect pharmacokinetics of drugs.

Variable	Young Adults (20–30 years)	Older Adults (60–80 years)
Body water (% of body weight)	61	53
Lean body mass (% of body weight)	19	12
Body fat (% of body weight)	26–33 (women)	38–45
	18–20 (men)	36–38
Serum albumin (g/dL)	4.7	3.8 → more free drug ↓ more effect + elimination
Kidney weight (% of young adult)	(100)	80
Hepatic blood flow (% of young adult)	(100)	55–60

drugs that undergo 1st pass effect are dangerous in elderly because the dose that usually get metabolized will ↓ → more active drug

Common Physiological Changes Associated with Aging

include:

a) **Reduced functional reserve capacity.**
b) **Reduced ability to maintain homeostasis, making them susceptible to de-compensation in stressful situations.**

Examples of such impaired homeostatic mechanisms:

1) Postural or gait stability
2) Orthostatic blood pressure responses
3) Thermoregulation
4) Cognitive reserve ↓
5) Bowel or bladder function.

Changes in pharmacoKinetics

Absorption

- Absorption by Passive diffusion: unchanged (depends on the drug itself)
- Absorption by Active transport ↓ (B_{12}, Ca^{++}, Iron, Mg^{++})
- First-pass effect ↓ → Bioavailability of Labetolol, Propranolol ↑ → we need to ↓ dose.
  → Pro-drugs (Enalapril, Codeine): Convergence to its active form ↓ → ↓ bioavailability → ↑ dose
- In case of Atrophic gastritis \ Use of acid-lowering agents → ↓ acidity → Acidic drugs (Conazoles, Iron, Digoxin, Penicillin) will be less soluble since they need to be in a lipophelic unionized state → ↓ bioavailability

Distribution

1. **Altered plasma protein concentrations.** (↓)
2. **Individual body composition (body fat and intracellular fluid content).**
3. **Decreased muscle and tissue mass.**
4. **Reduced blood flow to tissues and organs.**
5. **Active uptake into tissues may be influenced by ageing.**

- BBB disturbed → ↑ concentration of drugs & toxins in brain.
- If a drug is Extensively bound to plasma protein → ↑ free fraction (the active form + faster elimination)
- ↓ distribution of water-soluble drugs (Ethanol, Gentamycin)
- ↑ distribution of Lipophilic drugs (Benzodiazepine, Rifampin, Metronidazole)
- Digoxin → distributed in muscles → ↑ free fraction

Metabolism

- **Hepatic metabolism of drugs depends on liver perfusion, activity and capacity of drug metabolizing enzymes, and protein binding.**

↳ All ↓ with aging.

Affect → Drugs with high hepatic extraction ratio (depends on hepatic Blood flow → flow ↓ with age): Propranolol, amitriptyline, Diltiazem, Lidocaine, Metoprolol, Morphine, & Verapamil.

Elimination

→ ↓ GFR → drugs eliminated by kidney will accumulate → we must ↓ dose depending on accurate CL_{cr} (Creatinine clearance) (Not eGFR)

If CL_{cr} < 30 Avoid → Colchicine, Co-trimoxazole (for UTI), Glyburide (for DM), Nitrofurantoin, Probenecid, Spironolactone, Triamterene (K+ sparing diuretics).

Reduce dose of → Acyclovir, Amantadine, Ciprofloxacin, Gabapentin (for seizure), Ranitidine (Acid lowering agent), Aminoglycosides, Vancomycin.

→ will cause exaggerated pharmacological effects.

Serum Cr is a poor indicator of renal function, as it's produced by muscles, & m. mass is ↓ in elderly

Changes in pharmacodynamics

- ↑ sensitivity to CNS drug effects [Benzodiazepines, Opioids, General anesthetics, Lithium, Antipsychotics, Anticholinergics]
  ↳ due to change in size & weight of brain, Altered BBB, change in neurotransmitter systems (ex: ↓ Dopamine transporters & receptors)
- Antihypertensive drugs → ↑ risk of orthostatic Hypotension (due to ↓ blood volume + Damaged baroreflex)
- CCB → ↑ risk of Hypotension & Bradycardia
- β-blockers → ↑ risk of Hypotension
- Diuretics → ↓ effectiveness
- Warfarin → ↑ risk of Bleeding

Proposed changes leading to altered pharmacodynamics of drugs may include: → Possibilities only → Not imp.

1. Changes in drug concentration at the receptor.
2. Changes in receptor numbers.
3. Changes in receptor affinity.
4. Post-receptor changes.
5. Age-related changes in homeostatic mechanisms.

Drug-Related Problems in elderly:

★ Preventable ⊖ve outcomes: . Withdrawal effects . Therapeutic failure . ADRs

★ RF: > Polypharmacy
> Inappropriate prescribing (wrong dose & duration, Duplication, Drug interactions, Prescribing drugs that should be avoided)
> Underuse
> Non-compliance (due to ADR, complex regimens, Misunderstanding, cost, Dysmobility, Dementia, Social factors (→ depression, living alone) ..)

Assessing & Monitoring drug therapy:

1_ Compare Problems' lists Vs Drug lists: If a drug is not indicated, not effective, duplicated, or its risks > benefits.

2_ If a chronic condition's outcome is not receiving an EBM to improve it.

3_ Monitor effectiveness & toxicity: Amiodarone → hepatotoxic + Contain Iodine monitor→ LFT + TSH
Antiepileptics, Lithium monitor→ Serum drug level
ACEi & ARBs, Diuretics monitor→ Serum K^+ level
Hypoglycemics monitor→ Glucose & HbA1c
Antipsychotics monitor→ Extrapyramidal ADRs
Warfarin monitor→ PT + INR.

4_ Document problems + Formulate a therapeutic plan: taking into account: Time into therapeutic benifit (depends on $T_{1/2}$ & therapeutic steady state), treatment target, Medication regimen complexity, & goals of care.

5_ Team-based management.

6_ Enhance Compliance: Set a schedule that fits the patient's lifestyle, Prescribe generic agents to ↓ cost, Easy-to open bottles, Easy to swallow forms, Provide oral + written drug info, Involve care givers.

7_ Asses Drug-Disease interaction:

★ Anticholinergics interact with→ BPH (both cause Urinary retention → UTI), Dementia or Cognitive impairement (ARD)
★ Antipsychotics → have extrapyramidal manifestation → Hx of falls, Parkinson's disease
★ Metoclopramine → Parkinon's disease.
★ CCB → Heart failure. ★ Aspirin → PUD (will ↑ bleeding ulcers) ★ NSAIDs → PUD, HF, Renal failure.

Potentially Inappropriate Medications in Older adults:

★ Anticholinergics, Antihistamies ($H_1\ominus$) Rationale→ Reduced elimination in older adults → Confusion, Constipation, Dry mouth, & Urine retention.
★ Nitrofurantoin → Potential for pulmonary toxicity & fibrosis, Hepatotoxicity, & peripheral neuropathy.
★ α-blockers (Can be given as "slow release") → high risk of ADR, orthostatic Hypotention, CNS adverse effects.
★ Immediate-release nifedipine (CCB; in HTN, Angina) → ↑ ischemia in heart & periphery → Hypotention + MI
★ Amiodarone (antiarrhythmic) → many ADR.
★ Antidepressants → Anticholinergic, Sedation, Orthostatic hypotension, MI.
★ Antipsychotics → ↑ risk of CVA, cognitive decline, Dementia, Mortality.
★ Barbiturates & Benzodiazepines → long $T_{1/2}$ → Dependence, Tolerance, Sedation, Cognitive impairement, Delirium, Falls, & Fractures.
★ Insulin sliding scale → ↑ risk of hypoglycemia.
★ Long acting Sulfonylureas → ↑ risk of prolonged hypoglycemia.
★ Metoclopramide → ↑ risk of extrapyramidal ADR, & dyskinesia.
★ PPI → Abolish acid secretion for 24 h → risk of infec° → Risk of C.difficile infec°.
★ Opioid, Meperidine, Pethidine → ↑ risk of neurotoxicity, delirium, & respiratory depression.
★ NSAIDs → ↑ risk of PUD, CVD & cardiac toxicity, & Renal failure
★ Central muscle relaxants (Cyclobenzaprine, Orphenadrine) → anticholinergic effects, Sedation, ↑ risk of falls & fractures.