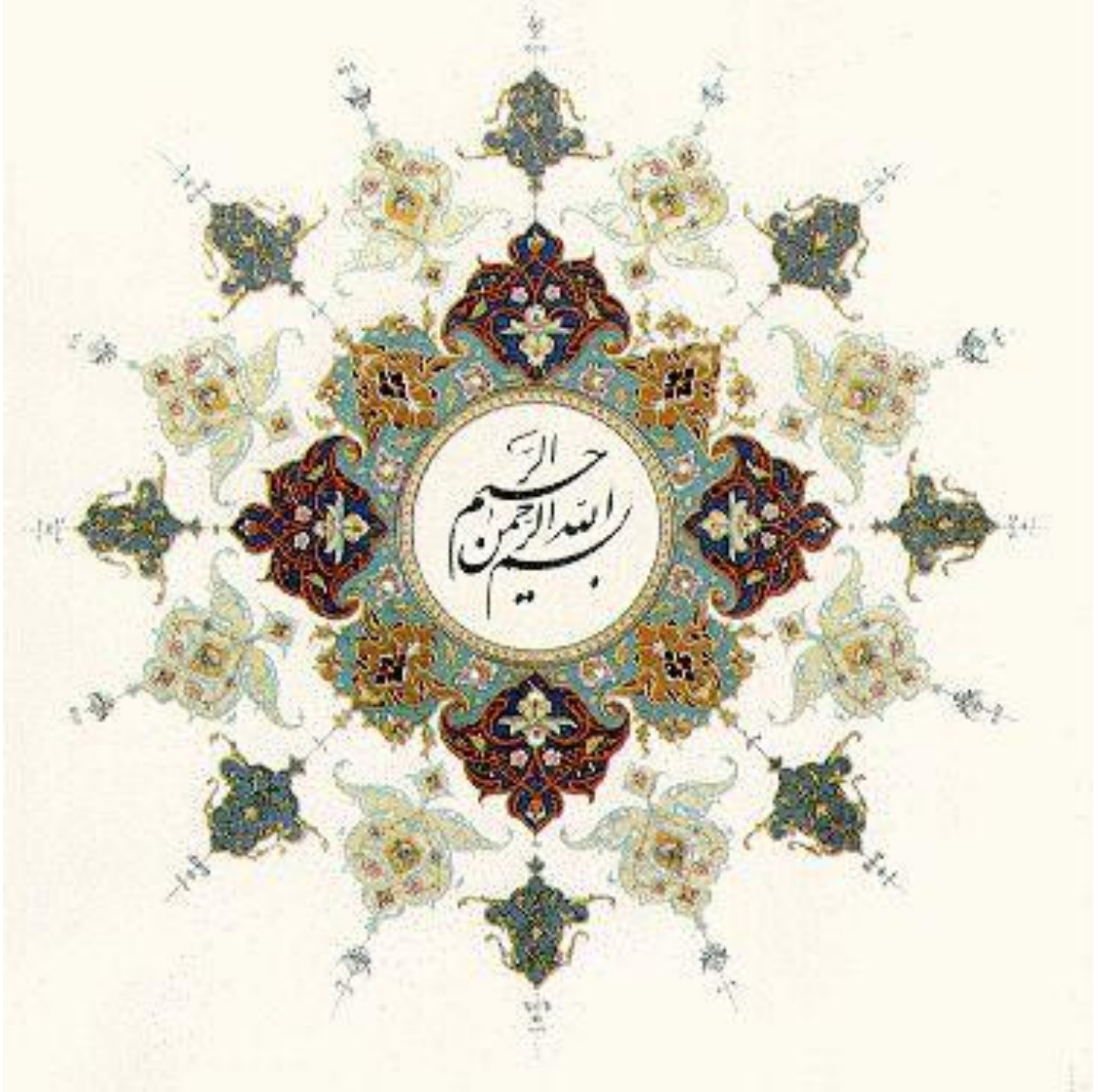
بسم الله الرحمن الرحیم

Geriatric Pharmacotherapy

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Problems in geriatric drug therapy

- Taking more medications
- Major drug studies performed on individuals < 55 yrs
- Premarketing drug trials
- Effect of aging on drug metabolism
- Alteration of drug response among patients

Polypharmacy

- 5 or more drugs
- Greater risk of ADR
- Greater potential for drug interactions
- Independent risk factor for hip fracture
- Prescribing cascades
- Low adherence

Geriatric drug therapy

- General rules: ½ or 1/3 of the usual dose
- ADR rate: twice
- ADR symptoms: subtle: falling, altered cognition, sedation, confusion, constipation, decreased appetite, thrive
- Significant ADRs : narrow therapeutic index or saturable hepatic metabolism: e.g phenytoin, warfarin, theophylline
- Increase risk of ADR in: multiple disease states, complicated drug therapy, poor compliance, age related changes

Frequency of adverse drug events and preventable adverse drug events by drug class

Drug class	Total adverse drug events (n = 815) N (percent)	Preventable adverse drug events (n = 338) N (percent)
Warfarin	121 (15)	42 (12)
Atypical antipsychotics	92 (11)	42 (12)
Loop diuretics	69 (8)	33 (10)
Opioids	51 (6)	26 (8)
Antiplatelets	46 (6)	23 (7)
ACE inhibitors	45 (6)	27 (8)
Antidepressants	43 (5)	25 (7)
Laxatives	43 (5)	16 (5)
Benzodiazepines (intermediate acting)	39 (5)	30 (9)
Insulins	37 (5)	18 (5)

Only drug classes with the frequency of adverse drug events of 5 percent and more are presented. Some adverse drug events were associated with more than one drug class.

Frequency of adverse drug events by type

Type	Total adverse drug events (n = 815) N (percent)	Preventable adverse drug events (n = 338) N (percent)
Neuropsychiatric	199 (24)	97 (29)
Hemorrhagic	159 (20)	53 (16)
Gastrointestinal	140 (17)	55 (16)
Renal/electrolytes	80 (10)	40 (12)
Metabolic/endocrine	64 (8)	35 (10)
Cardiovascular	36 (4)	15 (4)
Dermatologic	36 (4)	4 (1)
Extrapyramidal symptoms	30 (4)	7 (2)
Fall with injury	21 (3)	17 (5)
Fall without injury	21 (3)	11 (3)
Infection	19 (2)	1 (<1)
Syncope/dizziness	16 (2)	8 (2)
Anticholinergic	9 (1)	3 (1)
Ataxia/difficulty with gait	9 (1)	5 (2)
Hematologic	8 (1)	3 (1)
Respiratory	6 (1)	4 (1)
Anorexia	3 (<1)	2 (<1)
Functional decline	3 (<1)	2 (<1)
Hepatic	1 (<1)	1 (<1)

Adverse drug events could manifest as more than one type. Neuropsychiatric events include oversedation, confusion, hallucinations, and delirium. Anticholinergic effects include dry mouth, dry eyes, urinary retention, and constipation.

Other Drug Therapy Problems

- Affordability

Affects 30% of patients

Higher non compliance rates

Higher for patients with multiple co-morbidities

- Dose availability

Required lower doses

Splitting tablets

Capsules

Drug-Drug Interactions

- Increased risk
- Warfarin
- Other most interactions with glyburide, digoxin, ACE-Inhs

Age related physiologic changes in relation with kinetics of drugs

- Elevated GI pH
- Delayed gastric emptying
- Decreased GI mobility/ intestinal blood flow/ absorptive surface area
- Reduced gastric secretion

Consequences of Delayed Gastric Emptying

- More contact time for potentially ulcerogenic drugs (e.g. NSAIDs, bisphosphonates)
- Antacid drug interaction (increased time for binding)
- Increased absorption of poorly soluble drugs
- Higher incidence of diarrhea and a delay in onset action of basic drugs

Table 5-1. Physiologic Changes with Aging that May Affect Pharmacokinetics[6,62]

Process	Physiologic Effect
Absorption	Reduced gastric acid production Reduced gastric-emptying rate Reduced GI motility Reduced GI blood flow Reduced absorptive surface
Distribution	Decreased total body mass Increased percentage of body fat Decreased percentage of body water Decreased plasma albumin Disease-related increase in alpha-1-acid glycoprotein Altered relative tissue perfusion Altered protein binding
Metabolism	Reduced liver mass Reduced liver blood flow Reduced hepatic metabolic capacity Reduced enzyme activity Reduced enzyme induction
Excretion	Reduced renal blood flow Reduced glomerular filtration Reduced renal tubular secretory function
Tissue sensitivity	Alterations in receptor number Alterations in receptor affinity Alterations in second messenger function[a] Alterations in cellular response Alterations in cellular nuclear response

Age related pharmacokinetic changes

- Delayed absorption of transdermal patches: opioid patches
- Decreased IM absorption
- Using controlled released drugs
- Effect of clinical factors (e.g. CHF,…)

Protein Binding

- Albumin decreases to 3.5 g/dL after 80
- Residents of nursing homes: 3 g/dL or less
- AAG decreases
- Protein binding = major determinant of drug activity

Decrease of pr binding : increase of unbound (active) drug

Increased free fraction

NSAIDs in general (naproxen) and salicylates : higher gastric bleeding

- **Phenytoin: seizure control with lower doses**

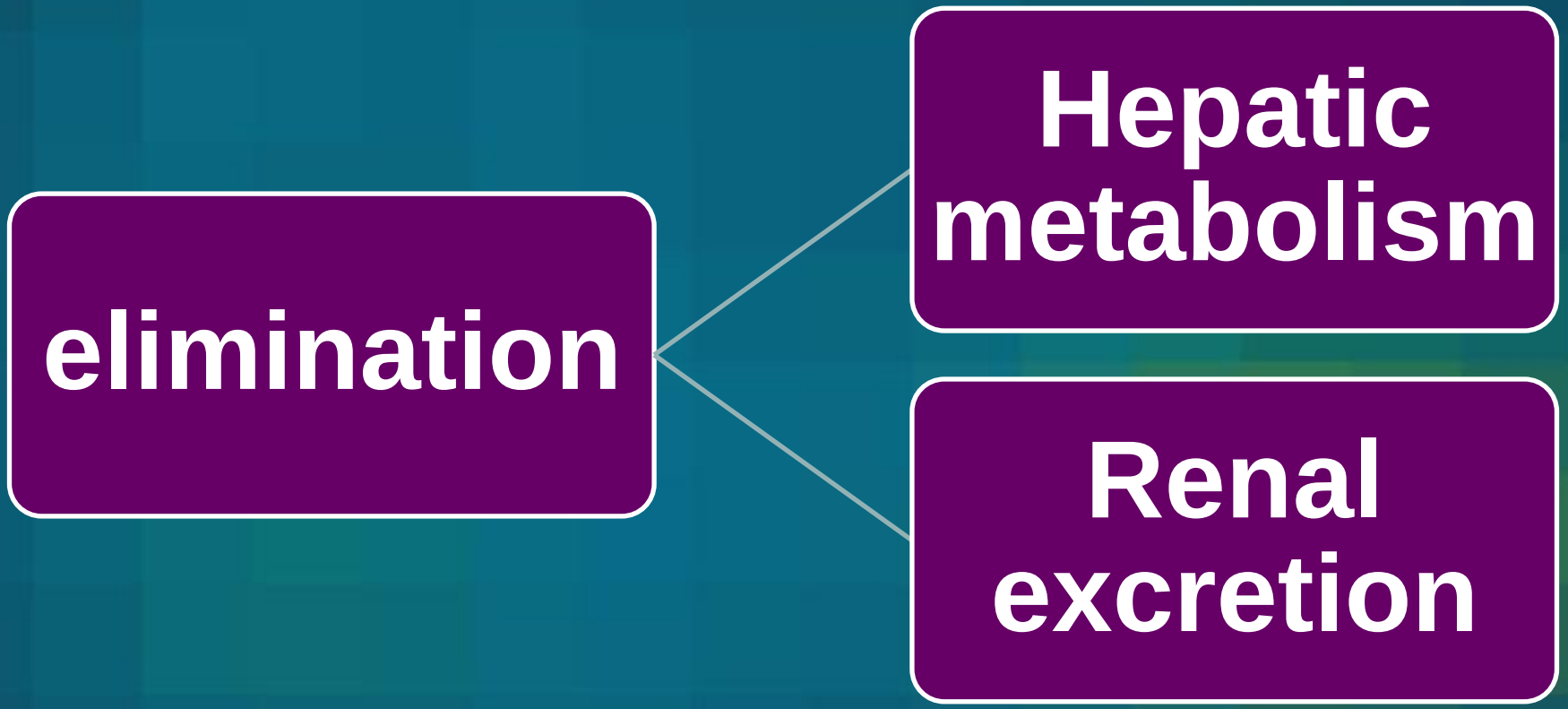
Select drugs with no or minimum change in protein binding

Lean Body Weight

- Total body water ↓
- Total body fat ↑
- Influence on the onset and duration of drugs
- Digoxin
- Alcohol, Morphine, Li

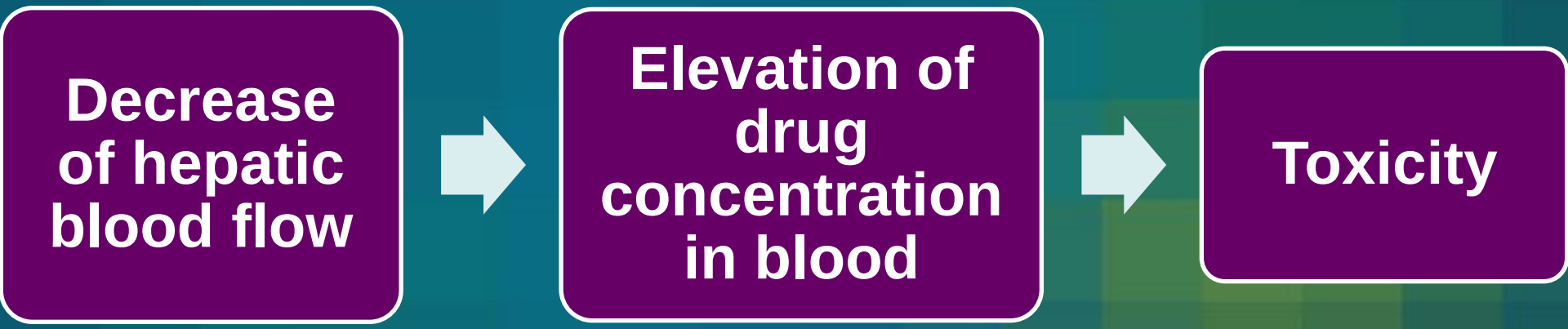
Volume of Distribution

- Vd of lipophilic drugs increases
- Delayed onset of action
- Accumulation in tissues: longer duration of action: toxicity
- TCAs, barbiturates, BDZs, CCBs, phenothiazines


elimination
Hepatic metabolism
Renal excretion

Hepatic metabolism

Beta blockers, lidocaine, narcotics



Renal Clearance

- Most age related declines in drug clearance is due to reductions in renal function
- Decrease of GFR to as much as 50%
- Serum Cr
- BUN
- Cl Cr
- Dose adjustment

Age related pharmacodynamic changes

- Decreased tolerance to the drug
- Decreased Ach, DA, 5HT
- Decreased enzymatic degradation of MAO
- Impaired baroreceptor response to BP changes
- Decreased responsiveness of beta-adrenergic receptors
- Increased pain tolerance
- Decreased Ab response to vaccination
- Decreased insulin sensitivity
- Decreased cortisol suppression

Pharmacodynamic changes

- Exaggerated pharmacologic response : barbiturates, BDZs, halothane, hydroxyzine, metoclopramide, warfarin
- Diminished pharmacologic response: beta blockers, beta agonists, CCBs
- Irreversible TD
- Difficulties of dose adjustment

Practical recommendations to reduce medical errors

1. Maintain an accurate list of all medications (drug name (generic and brand), dosage, frequency, route, and indication).
2. Advise periodic "brown bag check-ups." Instruct patients to bring all pill bottles to each medical visit; bottles should be checked against the medication list.
3. Patients should be made aware of potential drug confusions: sound-alike names, look-alike pills, and combination medications.
4. Patients should be informed of both generic and brand names
5. Community pharmacists

References

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- Geriatric Pharmacotherapy 2007
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