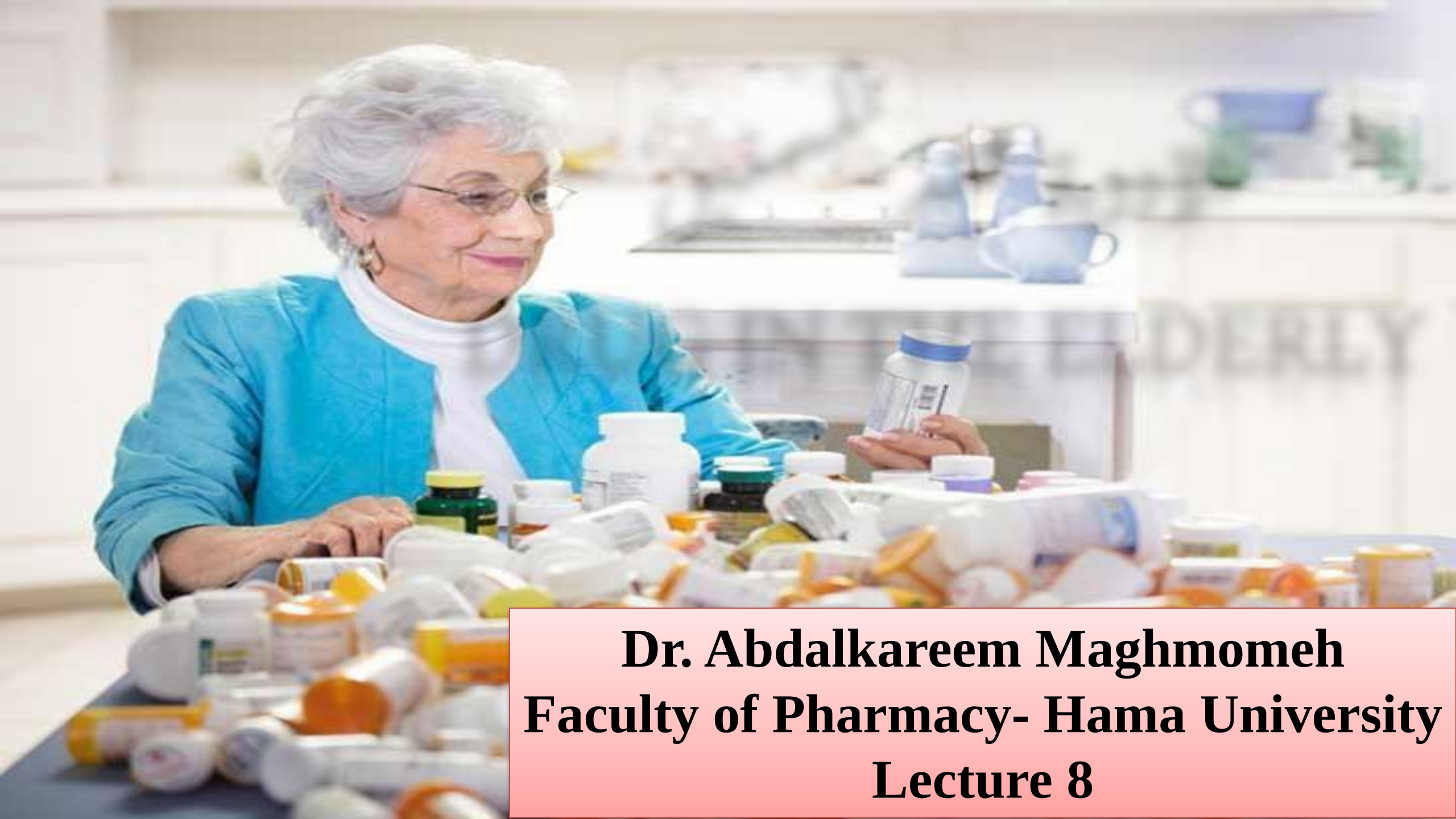

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Lecture 8

DEFINITION OF ELDERLY

Conventionally, “elderly” has been defined as a chronological age of 65 years old or older, while those from 65 through 74 years old are referred to as “**early elderly**” and those over 75 years old as “**late elderly.**

Why Geriatrics Pharmacology is Important

- Elderly population (> 65 yrs):
  - Constitute 13% of total population,
  - Purchase 33% of all prescription drugs
  - Consume 40% of OTCs
  - Thus, the elderly consume 3 times as much drugs as the younger population
- Elderly population is the fastest growing population in the US

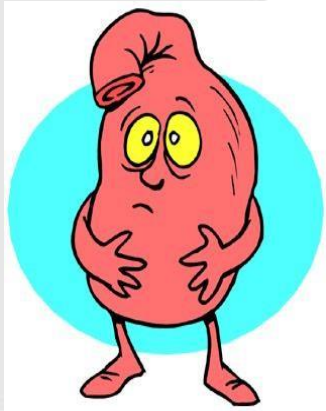
BASIC CONCEPTS

- Multiple **diseases**, multiple **drugs**, multiple **describers**.
- **Diseases** often chronic, progressive with adverse consequences
- Different **metabolisms** and **responses**
- Supplements, herbals, and OTC drugs
- Disease profile influenced by socioeconomic & emotional status
- **Symptoms may be silent**: no pain, no fever in infection or may be atypical & unrelated. Weak link organ symptoms: confusion, incontinence, depression, heart failure-Geriatric Syndromes

PHARMACOKINETIC CHANGES

Absorption

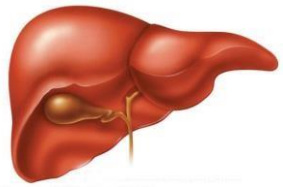
Changes	• ↓ swallowing; • ↓ gastric emptying; • ↑ gastric pH; • ↓ intestinal motility; • ↑ transit time; • ↓ absorptive surface; • ↓ mesenteric blood flow
Effects	↓ Rate of absorption*; Bioavailability may be altered *Worsened by anticholinergic drugs, antacids, or co-administration with food
Implications	• Onset of actions is delayed • Clinical effect is reduced if absorption is incomplete • Factors that reduce absorption should be minimized



Distribution

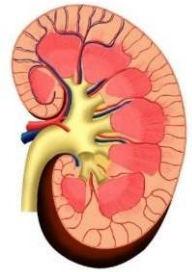
Changes	• ↓ muscle mass; • ↓ total body water; • ↑ total body fat
Effects	↑ Total body fat leads to increased Vd of most lipophilic drugs, resulting in ↑ t1/2 without change in s.s. Effect of decreased total body H2O increasing half-life of Li+ is offset by age-associated reduction in renal clearance
Implications	• Longer treatment interval is needed to reach s.s. • Single doses of agents have a decreased duration of action due to redistribution into fat stores.

METABOLISM



- **Slowed Phase I, cytochrome P450, reactions**
  - Oxidation, reduction, dealkylation
  - Warfarin and phenytoin levels may be higher because of altered metabolism
- **Phase II reactions are essentially unchanged**
  - Conjugation, acetylation, methylation
- **Drug-drug interactions**
  - Increased risk with increased number of drugs

EXCRETION



❖ Renal

- ✓ Renal clearance may be reduced (40-50%)))
- ✓ Serum creatinine may not be an accurate reflection of renal clearance in elderly patients.

❖ Active drug metabolites may accumulate

- ✓ Prolonged therapeutic action
- ✓ Adverse effects

Digoxin – lithium – aminoglycosides - vancomycin

Renal mass
Renal blood flow
GFR
Tubular excretion

Effects of Physiological Changes on pharmacokinetics In Elderly Subjects

Absorption	Metabolism
- Increased gastric ph - Delayed gastric emptying - Decreased splanchnic blood flow - Decreased intestinal mobility	- Decreased hepatic mass - Decreased hepatic blood flow - Decreased Phase I metabolism (Oxidative) - Unaltered phase II metabolism (Conjugation & Acetylation)
Distribution	**Elimination**
- Increased body fat - Decreased total body water - Decreased Serum albumin - Increased X-acidic glycoprotein - Cerebral flow	- Decreased Creatinine Clarence - Decreased GFR - Decreased tubular filtration - Creatinine

Action	With aging	Significance
Absorption/first pass	Reduced first pass metabolism (reduced liver mass, reduced blood delivery to liver)	Same amount of medication absorbed, but increased bioavailability of some drugs (eg. metoprolol, nortriptyline)
Volume of distribution	Increased body fat Decreased body water	Prolonged half life of fat soluble drugs (eg. diazepam) Increased serum concentrations of water soluble drugs (eg. digoxin, paracetamol)
Protein binding	Lower serum albumin in frail or unwell elderly	Increased free concentrations of protein bound drugs (eg. warfarin, phenytoin)
Metabolism	Reduced oxidative metabolism (liver) Unchanged conjugative metabolism (liver)	Prolonged half life, higher steady state concentrations of some drugs (eg. diazepam, metoprolol, phenytoin)
Excretion	Reduced with decreased glomerular filtration rate (GFR) and tubular excretion	Prolonged half life, higher steady state concentrations of some drugs or metabolites (eg. digoxin, cephalexin, morphine)

PHARMACODYNAMICS

Pharmacodynamic changes with age include receptor alterations(change in number and sensitivity), impaired signal transduction and decreased homeostatic regulation.

Response decreased	Response increased
Response to β agonists and β blockers is reduced due to reduced number of β receptors	•Reduced sensitivity of baroreceptors ,more chances of orthostatic/postural hypotension •Enhanced response to sedative-hypnotics and more respiratory depression . •Intolerance to digitalis •Greater response to coumarin

COMPLIANCE IN THE ELDERLY

- Incomplete compliance is extremely common in elderly people. due to:
- a failure of memory or to not understanding how the drug should be taken.
- many patients store previously prescribed drugs in the medicine cupboard which they take from time to time.
- It is essential that the drug regimen is kept as simple as possible and explained carefully.
- improve methods of packaging to reduce over- or under-dosage.
- Multiple drug regimens are confusing and increase the risk of adverse interactions

Table 4. Selected High-Risk Drugs

Drug	Potential Harm
Insulin and sulfonylureas	Hypoglycemia
Warfarin	Gastrointestinal, intracranial bleeding
Digoxin	Impairment of cognition, heart block
Benzodiazepines	Falls
Diphenhydramine, other first-generation antihistamines	Impaired cognition, urinary retention in men
Antipsychotics	Death, pneumonia

AGS BEERS CRITERIA

- The American Geriatrics Society
- Originally conceived by Dr. Mark Beers
- Published in 1991, revised in 1997, 2002, and 2012.
- Consensus-based, but statistical association with adverse drug events
- Adopted for nursing home regulation.
- Does not account for the complexity of a patient's entire medication regimen.

BEERS CRITERIA: BENZODIAZEPINES

- **Increased sensitivity for older adults**
  - Slowed metabolism, especially long-acting agents
  - Similar neurocognitive effects to alcohol
- **Increased risk of adverse clinical events**
  - Falls and fractures
  - Cognitive impairment
- **Avoid if possible**
  - Appropriate if being used for seizures, alcohol withdrawal, severe anxiety
  - If necessary, use lowest dose possible

BEERS CRITERIA: PAIN MEDICATIONS

- **Non–COX-selective NSAIDs: oral Aspirin >325 mg/day - Diclofenac - Ibuprofen - Ketoprofen - Mefenamic acid**
  - ➢Avoid chronic use unless other alternatives are not effective and patient can take gastro protective agent ((proton pump inhibitor)
  - ➢Increases risk of GI bleeding/peptic ulcer disease in high-risk groups, including those
  - ➢≥75 years old or taking oral or parenteral corticosteroids, anticoagulants, or antiplatelet agents. Use of proton pump inhibitor reduces but does not eliminate risk.
- **Indomethacin and Ketorolac**
  - ➢Avoid
  - ➢Higher risk of GI, renal, and CNS effects

BEERS CRITERIA: CARDIOVASCULAR DISEASE

- **Alpha1 blockers**
  - Avoid use as an **antihypertensive**.
  - High risk of orthostatic hypotension; not recommended as routine treatment for hypertention.
- **Alpha agonists**
  - Avoid **clonidine** as a first-line antihypertensive.
  - High risk of adverse CNS effects; may cause bradycardia and orthostatic hypotension;
  - Not recommended as routine treatment for hypertension.
  - Hypertension; alternative agents have superior risk/ benefit profile.

BEERS CRITERIA: CARDIOVASCULAR DISEASE

- **Nifedipine, immediate release**
  - Avoid.
  - Potential for hypotension; risk of precipitating myocardial ischemia.

- **Spironolactone >25 mg/day**
  - Avoid in patients with heart failure or with a Cr Cl <30 mL/min.
  - In heart failure, the risk of hyperkalemia is higher in older adults if taking >25 mg/day.

DIURETICS

- Diuretics are more likely to cause adverse effects

postural hypotension, **glucose intolerance** and **electrolyte disturbances**

- Clinically important **hypokalemia** is uncommon with low doses of diuretics, but plasma potassium should be checked after starting treatment.
- If clinically important hypokalemia develops, a thiazide plus potassium can be considered
- there is a risk of hyperkaliemia due to renal impairment, especially if an ACE inhibitor and/or angiotensin receptor antagonist and aldosterone antagonist are given together with the diuretic for hypertension or heart failure.
- Thiazide-induced **gout and glucose intolerance** are important side effects

(ACEIS / ((ARBS)

- effective and usually well tolerated in the elderly.
- **hypotension, hyperkaliemia and renal failure** are more common in this age group.
- serum creatinine levels checked before and after starting treatment.
- ARB do not cause the dry cough that is common with ACEI.

DIGOXIN

Digoxin >0.125 mg/day

Avoid.

In heart failure, higher dosages associated with no additional benefit and may increase risk of toxicity

decreased renal clearance may increase risk of toxicity.

BEERS CRITERIA: DIABETES MELLITUS

- **Insulin,**
  - Avoid.
  - Higher risk of hypoglycemia without improvement in hyperglycemia management regardless of care setting
- **Sulfonylureas**
  - long-duration Chlorpropamide Avoid.
  - Chlorpropamide prolonged half-life in older adults; can cause prolonged hypoglycemia
  - higher risk of severe prolonged hypoglycemia in older adults.

PRACTICAL ASPECTS OF PRESCRIBING FOR THE ELDERLY

- Take a **full drug history** which should include any adverse reactions and use of over-the- counter drugs.
- Know the **pharmacological action** of the drug employed.
- Use the **lowest effective dose**.
- Use the **fewest possible number of drugs** the patient needs.
- Consider the potential for **drug interactions** and co-morbidity on drug response.

PRACTICAL ASPECTS OF PRESCRIBING FOR THE ELDERLY

- Drugs should seldom be used to treat symptoms without first discovering the cause of the symptoms (i.e. first diagnosis, then treatment).
- Drugs should not be withheld because of old age, but it should be remembered that there is no cure for old age either.
- A drug should not be continued if it is no longer necessary.
- Do not use a drug if the symptoms it causes are worse than those it is intended to relieve.
- It is seldom sensible to treat the side effects of one drug by prescribing another.

THANK YOU FOR LISTENING