IMPACT OF AGING ON MEDICATION USE AND DEPRESCRIBING

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DISCLOSURE

- I have had no financial relationship over the past 24 months with any commercial sponsor with a vested interest in this presentation.

Pharmacist Objectives

1. Describe the functional changes that occur in the normal aging process

2. Discuss common medications typically identified for deprescribing

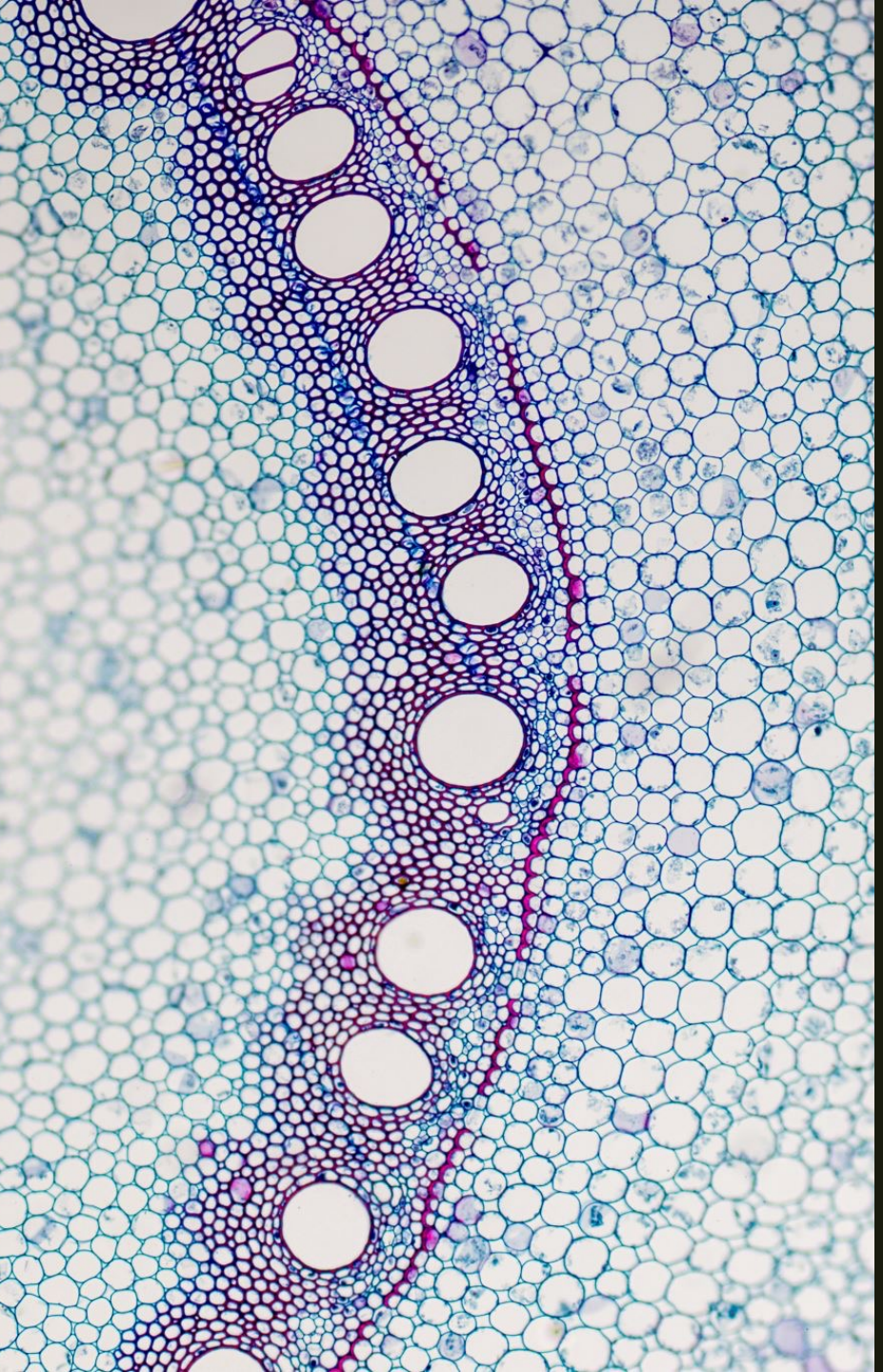
3. Review practices for medication transitions and quality of life considerations

Pharmacy Technician Objectives

1. Describe the functional changes that occur in the normal aging process
2. Discuss common medications typically identified for deprescribing
3. Review practices for medication transitions and quality of life considerations

THE NORMAL AGING PROCESS

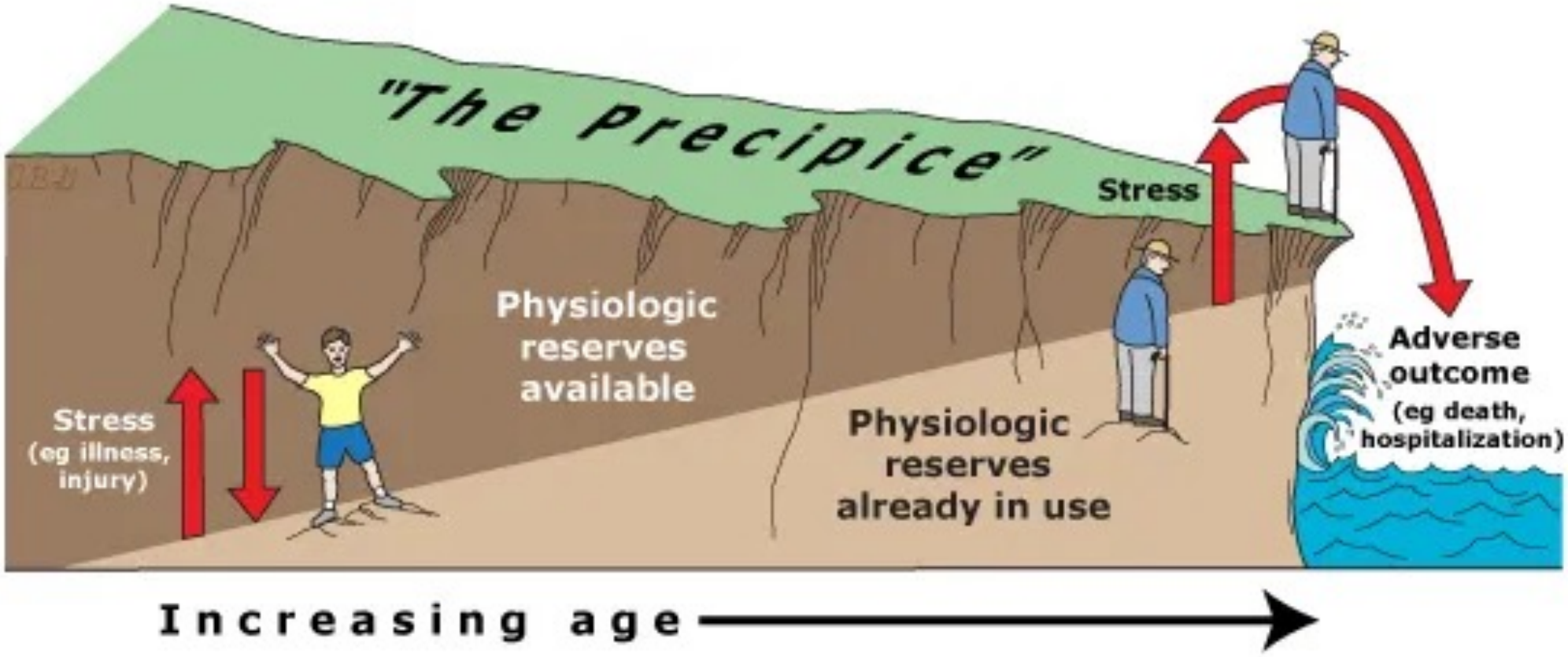
Aging is not a disease, but is a significant risk factor for disease



HOMEOSTASIS X AGING = HOMEOSTENOSIS

- Homeostasis: internal self-regulating of an organism by using physiological processes to survive external challenges and maintain a steady state
- Aging: micro and macro structural and functional changes at the cellular level of an organism
- Homeostenosis: due to aging, self-regulation reserves diminish, leading to increased vulnerability when faced with an external challenge

Homeostenosis

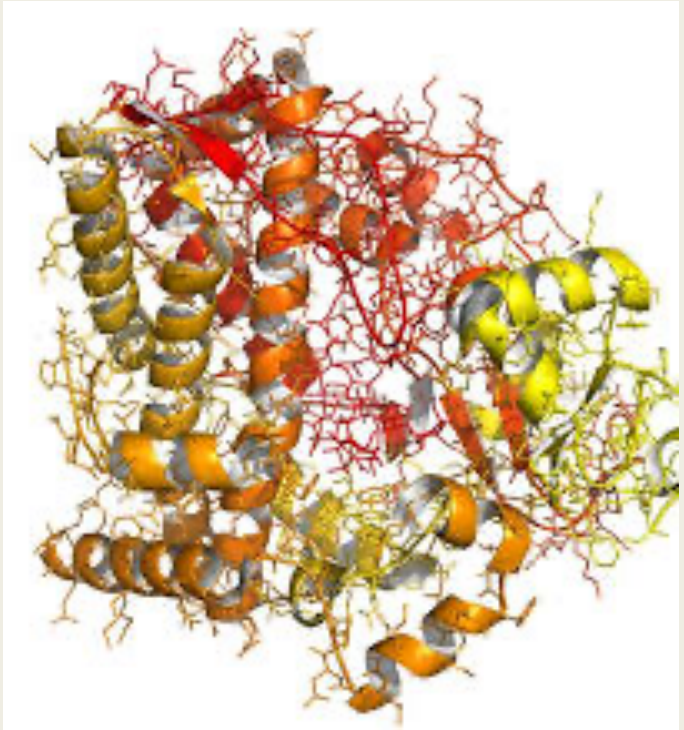


Aging Digestive System

- Gums recede, saliva production decreased, esophageal muscle weakened
  - *Impaired swallowing*
- Decreased gastric emptying and prostaglandin synthesis
  - *Increased sensitivity to gastric irritants (nonsteroidal anti-inflammatory drugs (NSAIDs), bisphosphonates)*
- Small intestine villi atrophied and mucosa thickened
  - *Less absorption of some vitamins and minerals*
- Large intestine contraction altered; motility decreased
  - *Constipation common*
- Anal sphincter tone decreased
  - *Fecal incontinence more likely*

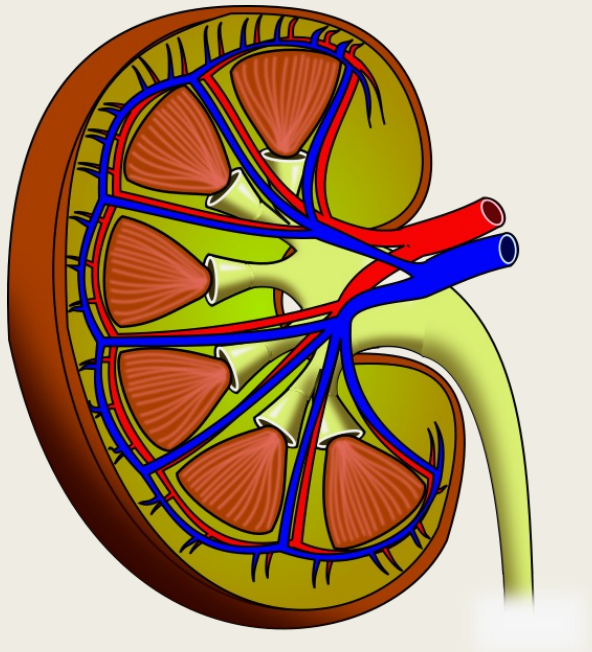
Aging Hepatic System

- Liver mass decreased 20-40% and liver blood flow decreased up to 50%
  - *Affects Phase 1 first pass metabolism of medications*
- Decreased LDL cholesterol metabolism in liver
  - *Higher serum LDL levels*
- Cytochrome P450 content, responsible for metabolizing drugs, altered
  - *Metabolic clearance of drugs is 20-40% slower!*
- Reduced production of Vitamin K dependent clotting factors
  - *Lower doses of vitamin K antagonists required*



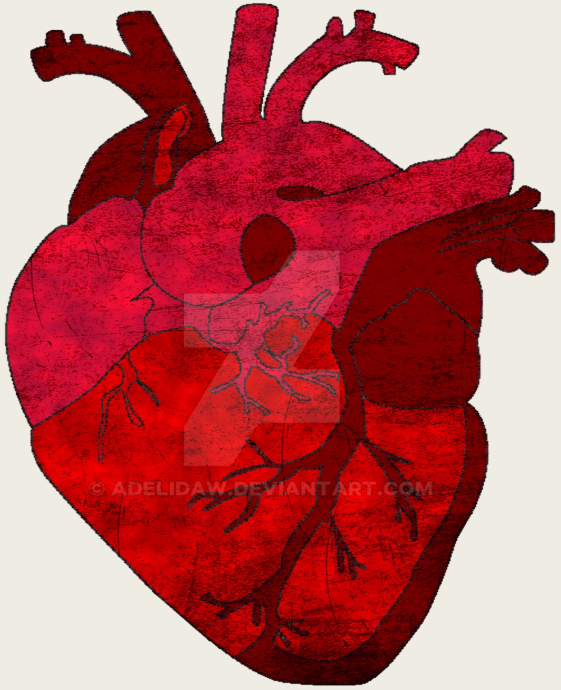
Cytochrome P450

Aging Renal System



- Kidney size reduced
- Nephron number reduced
  - *Higher risk for acute kidney injury*
- Fat and fibrosis replace functioning tissues
- Decreased kidney blood flow
- Renal cysts occur
- Glomerular filtration rate (GFR) and Creatinine Clearance (CrCl) decreased
  - *Medication dose adjustments required for certain medications (especially those with a narrow therapeutic index)*
  - *Over 50% of adults over 70 years old have chronic kidney disease (CKD), diagnosed by GFR less than 60 ml/min/1.73 m2*

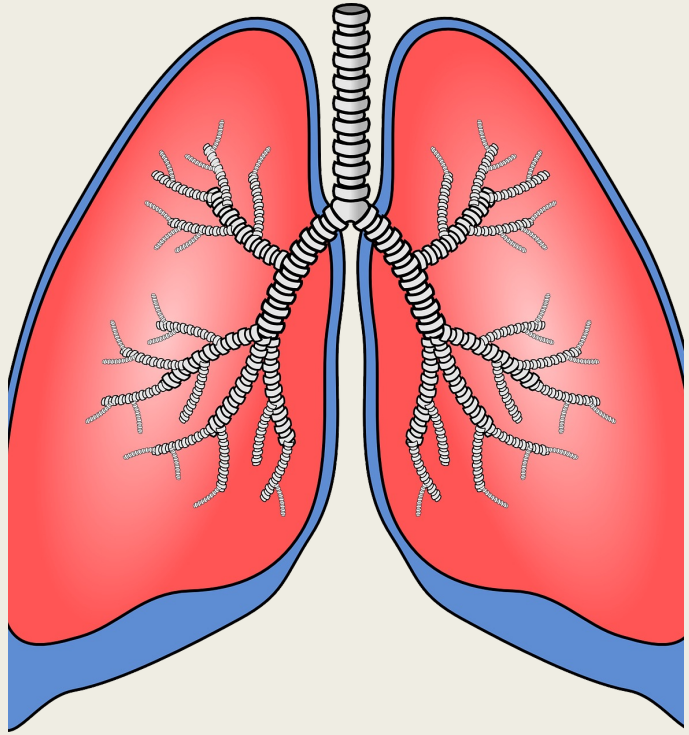
Aging Cardiovascular System



- Aorta and great arteries stiffened
- Left ventricle stiffened and thickened
- Aortic and mitral valve thickened
- Less variability in heart rate and blood pressure
- Small decrease in resting heart rate but large decrease in maximum heart rate in response to stressors
  - *Lots of reserves utilized to maintain resting cardiovascular function*
  - *Mortality and probability of heart failure after a myocardial infarction increased with age*
    - HOMEOSTENOSIS!

Aging Respiratory System

- Alveolar ducts enlarged, 1/3 of surface area per volume of lung tissue lost
  - *Decreased area for gas exchange*
- Chest wall stiffened
- Diaphragm less efficient
  - *Abdominal muscles required for inhalation (difficult to use sitting down)*
- Maximum inspiratory pressure and peak inspiratory flow decreased
  - *Difficult to properly use dry powder inhalers*
- Cough less intense, mucus clearance slowed
- Gene expression of angiotensin-converting enzyme 2 (ACE2), the SARS-CoV-2 receptor, increased in lung with age



Aging Musculoskeletal System

- Muscle mass decreased in relation to body weight
  - *impaired balance and motility*
  - *Increased insulin resistance*
- Increased fat relative to muscle
  - *Water-soluble drugs, ie., digoxin, have decreased volumes of distribution (higher serum levels)*
  - *Lipid soluble drugs, ie., diazepam, have increased volumes of distribution (prolonged half-life)*

- Bone mass decreased
- Osteoblast number and activity declines
- Aging increases probability of fracture and rate of repair is slowed after fracture
  - HOMEOSTENOSIS!

Weightbearing exercise can help increase bone mineral density and prevent age related bone loss!

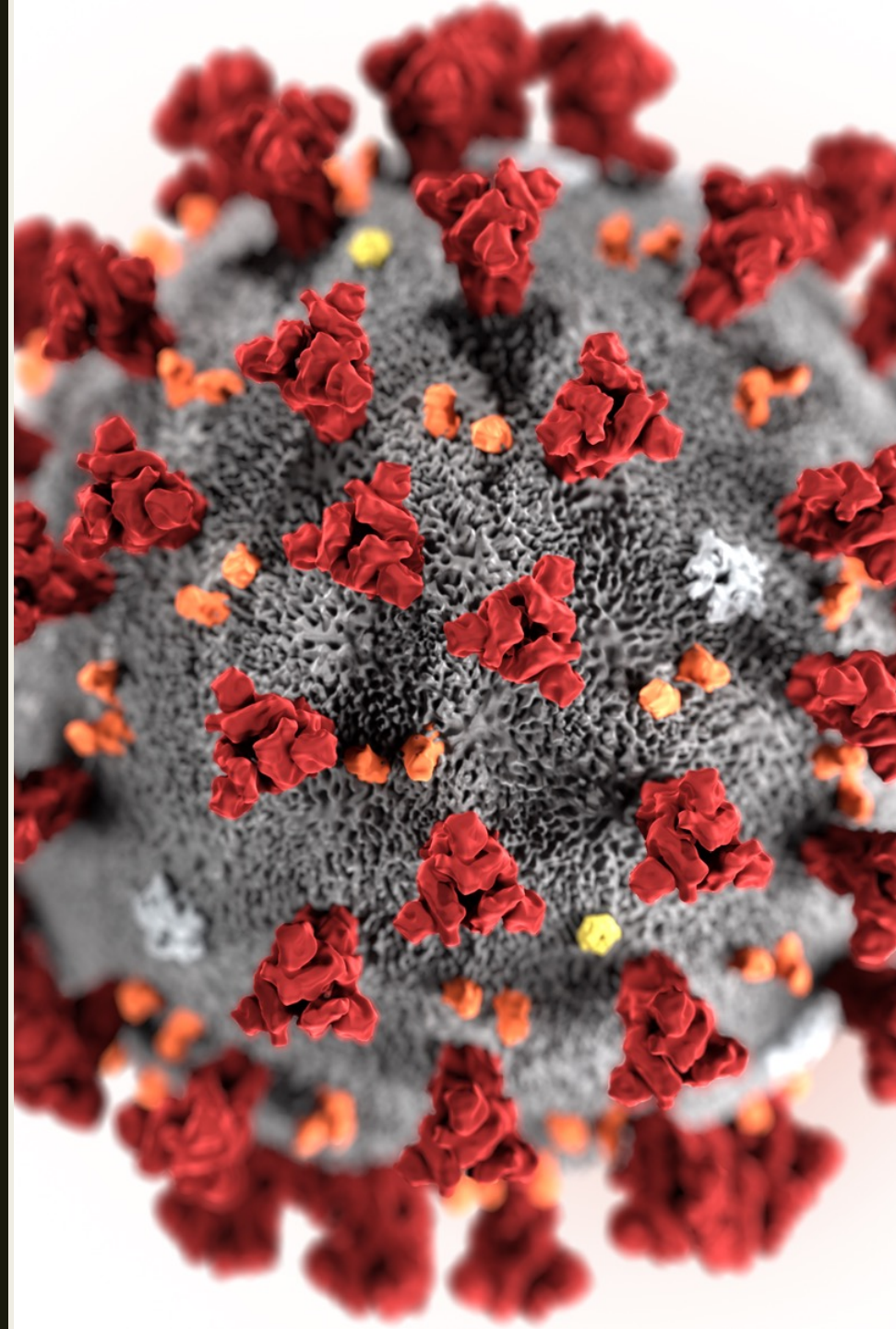
Aging Central Nervous System

- Neuron loss in cerebellum and cerebral cortex
- Acetylcholine availability decreases
- Dopamine decreases
- Brain volume decreases
- Processing speed decreases
- Working memory and executive function most affected by aging after age 60
  - *Difficulty adhering to complex medication regimens*

Engaging in social, leisure, and cognitive activities, learning new language, pursuing higher education may decrease risk of Alzheimer's Disease or delay onset and slow progress of normal aging.

Aging Immune System

- Lymphocytes (T and B) ability to work together to activity immune response decreases
  - *Less efficacy of vaccinations*
  - *Lower ability to fight new infections*
- Loss of precise regulation of inflammatory processes—cytokine profile shows a chronic, low level inflammatory state of “inflammaging”
  - *Increases mortality and morbidity*
  - *Increases risk of infections, malignancy, and autoimmune disorders*



ADDITIONALLY…

Hormonal, urinary, blood, skin, sight, hearing, smell, taste, etc., changes occur, affecting quality of life and thus mental health.

MEDICATION PROBLEMS IN ELDERLY

POLYPHARMACY

- The use of multiple medications, including both over-the-counter (OTC) and prescription medications
- Over 40% of elderly have 5 or more medications
- Associated with decreased physical and cognitive function
- May lead to nonadherence
- **THE SINGLE HIGHEST PREDICTOR OF ADVERSE DRUG EVENTS IN OLDER PATIENTS**

ADVERSE DRUG EVENTS (ADE)

- Drug-drug interactions
  - *Risk of bleeding with warfarin therapy increased with NSAIDs, selective serotonin reuptake inhibitors (SSRIs), certain antibiotics, etc.*
- Dose-related adverse drug events
  - *Dose of benzodiazepines related to risk for hip fracture in older adults*
  - *Failure to properly adjust dose for renal impairment*
    - 52% of elderly in community population with mild renal impairment were taking medications that required renal dosage adjustments
- Hospitalizations
  - *Nearly 100,000 ADE-related hospitalizations per year in elderly population*

PRESCRIBING CASCADE

- When a medication is started to treat a side effect of another medication
- Examples:
  - *Antiparkinson therapy started after movement side effects from antipsychotics or metoclopramide*
  - *Anticholinergic therapy for urinary incontinence developed from acetylcholinesterase inhibitor*
  - *Peripheral edema from calcium channel blockers treated with diuretic*

HIGH RISK MEDICATIONS & DEPRESCRIBING TARGETS

AMERICAN GERIATRIC'S SOCIETY: Beer's Criteria

- Tool for drug prescribing in elderly
- Five categories:
  1. *Those potentially appropriate in most older adults*
  2. *Those that should typically be avoided in older adults with certain conditions*
  3. *Drugs to use with caution*
  4. *Drug-drug interactions*
  5. *Drug dose adjustment based on kidney function*
- American Geriatric's Society advises clinicians to use common sense and good clinical judgment, understanding strict adherence not always appropriate
- Not for use in palliative care and hospice settings

DRUGS POTENTIALLY INAPPROPRIATE IN MOST OLDER ADULTS

- **ANTICHOLINERGICS!** (Diphenhydramine, doxylamine, meclizine, hydroxyzine, benztropine, paroxetine, amitriptyline, nortriptyline, dicyclomine, carisoprodol, metaxalone, cyclobenzaprine)
  - *Reduced clearance in elderly; increased risk of confusion, dry mouth, constipation, toxicity.*
- **NITROFURANTOIN**
  - *Potential for pulmonary toxicity, hepatotoxicity, and peripheral neuropathy; go with another alternative (especially for longer term use)*
- **INSULIN (SLIDING SCALE); SULFONYLUREAS** (glimepiride, glyburide)
  - *Higher risk of hypoglycemia*
- **PERIPHERAL ALPHA-1 BLOCKERS** (terazosin, doxazosin) **AND/OR CLONIDINE FOR HYPERTENSION**
  - *High risk of orthostatic hypotension; alternative agents have fewer adverse effects*
- **DIGOXIN**
  - *Avoid as first-line agent in atrial fibrillation; safer agents available for rate control*
  - *Reduced renal clearance can lead to toxicity*
  - *If used, avoid dosages over 0.125 mg/day*
  - *Avoid initiating in heart failure but use caution in deprescribing if already using*

DRUGS POTENTIALLY INAPPROPRIATE IN MOST OLDER ADULTS, cont.

- **BENZODIAZEPINES AND BENZODIAZEPINE RECEPTOR AGONISTS** (zolpidem, zaleplon, eszopiclone)
  - *Increased sensitivity and risk for delirium, falls, cognitive impairment, and motor vehicle crashes in older adults*
- **PROTON PUMP INHIBITORS**
  - *Risk of Clostridium difficile infection, GI malignancies, pneumonia, bone loss, and fractures*
  - *Limit use to 8 weeks unless used for appropriate indication*
- **ANTIPSYCHOTICS, both typical and atypical**
  - *Increased risk of stroke and greater rate of cognitive decline*
  - *Avoid, except in FDA approved indications (schizophrenia, bipolar disorder, Parkinson psychosis, major depressive disorder as adjunctive treatment, or antiemetic)*
- **ASPIRIN** for primary prevention of cardiovascular disease
  - *Avoid initiating aspirin and consider deprescribing*
  - *Risk of major bleeding increases*

DRUGS POTENTIALLY INAPPROPRITE IN MOST OLDER ADULTS, cont.

- **ANDROGENS, SYSTEMIC ESTROGENS**
  - *Avoid androgens due to risk of cardiac problems*
  - *Do not initiate systemic estrogen and consider deprescribing if already using due to carcinogenic potential and risk of heart disease, stroke, blood clots, and dementia*
  - *Vaginal estrogens for dryness are considered safe*
- **METOCLOPRAMIDE**
  - *Risk for extrapyramidal effects when used for more than 12 weeks*
- **Aspirin>325 mg/day and non-COX2 selective oral NSAIDs** (ibuprofen, naproxen, meloxicam, diclofenac)
  - *Increased risk of gastrointestinal bleeding (risk increases with duration of use)*
  - *May increase blood pressure and cause kidney injury*
  - *Proton pump inhibitors minimize risk for ulcer*

ANTICOAGULATION RECOMMENDATION SUMMARY (new in 2023)

- WARFARIN
  - *Avoid starting as initial therapy for treatment of venous thromboembolism (VTE) or nonvalvular atrial fibrillation unless other options are contraindicated*
  - *If been on warfarin long term with well controlled INR and no adverse effects, can consider continuing*
- RIVAROXABAN
  - *Avoid for long term treatment of nonvalvular a. fib or VTE*
- DABIGATRAN
  - *Use caution in selecting dabigatran over other DOACs for long term treatment of nonvalvular atrial fibrillation or VTE*

DRUGS THAT SHOULD TYPICALLY BE AVOIDED IN OLDER ADULTS WITH CERTAIN CONDITIONS

Condition	Medication/Class	Adverse Effect
Dementia	-Anticholinergics, benzos, and Z drugs -Antipsychotics	-Increased confusion -Risk of stroke and mortality
Heart Failure	-Verapamil, diltiazem; NSAIDs; Pioglitazone, rosiglitazone	-Fluid retention/exacerbate heart failure
Parkinson Disease	-Metoclopramide; antipsychotics (except quetiapine, clozapine, pimavanserin)	-Worsen Parkinsonian symptoms
Syncope	-Acetylcholinesterase inhibitors -Nonselective peripheral alpha-1 blockers -Antipsychotics; tertiary tricyclic antidepressants (chlorpromazine)	-Cause bradycardia which could be cause of syncope -Orthostatic hypotension -Increase risk of orthostatic hypotension and bradycardia

DRUGS TO USE WITH CAUTION

- **Dabigatran**—use with caution for treatment of venous thromboembolism or atrial fibrillation in adults 75 years or older
  - *Risk of gastrointestinal bleeding increased; use alternative (e.g., apixaban)*
- **Sulfamethoxazole-trimethoprim**—use with caution in patients on ACE inhibitor or ARB and decreased CrCl
  - *Increased risk of hyperkalemia*
- **Tramadol, SSRIs, serotonin-norepinephrine reuptake inhibitors (SNRIs), antipsychotics, diuretics, carbamazepine**—use with caution
  - *May cause hyponatremia or syndrome of inappropriate antidiuretic hormone secretion (SIADH)*
  - *Monitor sodium level closely upon initiation/change of dose*
- SGLT2 INHIBITORS (empagliflozin, dapagliflozin, etc.)
  - *Increased risk for urogenital infections*
    - Especially women within first month of initiating

DRUG-DRUG INTERACTIONS

DRUG/DRUG CLASS	DRUG/DRUG CLASS	ADVERSE EFFECT
Warfarin	Amiodarone, ciprofloxacin, macrolides (except azithromycin), sulfamethoxazole-trimethoprim, NSAIDS, SSRIs	Increased risk of bleeding
Anticholinergic	Anticholinergic	Increased risk of cognitive decline and falls/fractures
Phenytoin	Sulfamethoxazole-trimethoprim	Increased risk of phenytoin tox
RAS inhibitors (ACEI, ARB, etc)	Another RAS inhibitor or K sparing diuretic	Increased risk of hyperkalemia
Non-selective peripheral Alpha-1 blockers	Loop diuretics	Increased risk of urinary incontinence in older women
Opioids	Benzodiazepines, gabapentin, pregabalin	Increased risk of overdose
Antidepressants, antipsychotics, antiepileptics, benzodiazepines, benzodiazepine receptor agonists, opioids	Any combo of 3 or more of these CNS-active drugs	Increased risk of falls (all) and fractures (benzos and benzo receptor agonists)

DRUG DOSE ADJUSTMENTS BASED ON RENAL FUNCTION (and CrCl which action required)

- CIPROFLOXACIN <30
- SULFAMETHOXAZOLE-TRIMETHOPRIM <30
- NITROFURANTOIN <30
- CIMETIDINE <50
- FAMOTIDINE <50
- NIZATIDINE <50
- BACLOFEN eGFR <60
- NSAIDS <30
- AMILORIDE <30
- DOFETILIDE <60
- EDOXABAN15-50
- ENOXAPARIN <30
- FONDAPARINUX <30
- Not APIXABAN
- DABIGATRAN <30
- RIVAROXABAN <50
- LEVETIRACETAM <80
- GABAPENTIN <60
- PREGABALIN <60
- DULOXETINE <30
- TRAMADOL <30
- COLCHICINE <30
- PROBENACID <30
- SPIRONOLACTONE <30
- TRIAMTERENE <30

DEPRESCRIBING

DEPRESCRIBING

- The supervised process of reducing a patient's number of medications and/or dosages of medication in order to manage polypharmacy and prevent adverse drug events.
- Look to discontinue and/or reduce medications in which risks outweigh benefits **for the individual**
- Balance required between over and under prescribing
  - *Multiple medications often necessary to manage multiple disease states*
  - *No "one-size-fits-all" guide*
- Ideal for patients with multiple disease states, multiple medications, renal impairment, medication nonadherence, multiple prescribers and transitions of care, limited life expectancy, and/or dementia
- Proactive approach
  - *Common to reactively discontinue a medication after an ADE*
  - *Most important yet most challenging aspect of deprescribing*

DEPRESCRIBING: WHY

- Reduce medication burden
  - *Shown to reduce use of potentially inappropriate medications by up to 60%**
  - *Could improve adherence to remaining medications*
- Reduce risk of falls
  - *Decreased fall risk by 24%**
- Reduce risk of hospitalization and death
  - *Hospitalizations reduced by 36%**
  - *Death reduced by 26-38%**
- Improve cognitive function
  - *Anticholinergics, benzos, use of multiple CNS-active medications slow cognition*

*shown in systematic review and meta-analysis of nursing home settings with deprescribing interventions

DEPRESCRIBING: HOW

- **Step 1:** Obtain accurate and up-to-date list of all medications the patient is taking and the indications for each one.
  - *Include all over-the-counter, supplements, prescriptions, scheduled, and PRN medications*
  - *Include dose and frequency, indication, duration of use, adherence, comments from patient (difficulty swallowing, side effects, etc.)*

- **Step 2:** Consider patient's overall susceptibility to drug-induced adverse events
  - *Example: falls, cognitive impairment, hypoglycemia*
  - *Discuss with patient, family, caregivers, and providers– when appropriate*

DEPRESCRIBING: HOW

- **Step 3:** Assess each drug's benefit vs risk potential in the individual and identify drugs to deprescribe. Use Beer's Criteria as a tool, and look for the following:

- **MEDICATION WITHOUT A VALID INDICATION**
- **MEDICATION SUSPECTED OF CAUSING AN ADVERSE DRUG REACTION**
- **MEDICATION STARTED AS A RESULT OF A PRESCRIBING CASCADE**
- **INEFFECTIVE MEDICATION**
- **DRUG USED FOR PREVENTION IN A PATIENT WITH LIMITED LIFE EXPECTANCY**
- **A DRUG CONTRIBUTING TO SEVERE DRUG-DRUG INTERACTION**
- **COMPLEX DOSING REGIMEN**
- **MEDICATION WITH A SAFER ALTERNATIVE AVAILABLE**

DEPRESCRIBING: HOW

- **Step 4:** Communicate with patient, family, caregivers, and providers
  - *Get approval from prescribing doctor and primary care provider*
  - *Explain why the medication should be stopped, the process, and how the patient will be monitored*
  - *Reassure this is a trial and the medication can be restarted if necessary*
  - *Remind patient and family that deprescribing is not "giving up" or taking valuable therapy away—it is optimizing health*
  - *Discuss how the symptom or disease will be managed, if necessary, without the medication*
  - *Address all other fears and concerns!*

DEPRESCRIBING: HOW

- **Step 5:** Implement a discontinuation plan with patient, family, caregivers and healthcare professionals
  - *Stop one medication at a time*
  - *Taper when appropriate to avoid withdrawal reactions*
  - *Advise patient and caregivers to self-monitor*
  - *Document the plan*
  - *Follow-up*

MEDICATION CLASSES TO TAPER:
Benzodiazepines
Proton Pump Inhibitors
Antipsychotics
Glucose-lowering medications
Cholinesterase inhibitors
Antidepressants
Antihypertensives

GENERAL RULE TO TAPER DOSE OVER WEEKS TO MONTHS IF UNSURE OF WHETHER A MEDICATION CAN BE STOPPED ABRUPTLY

HURDLES TO OVERCOME

- Patient, family, prescriber reluctance: “I/they have been on this medication for years and never had a problem.”
  - *Explain how aging affects medication and the increased potential for adverse effects*
- Limited time
  - *Identify target patients for review*
  - *Set aside separate visits when possible*
  - *Initiate conversation during patient encounter (ie, medication pickup)*
  - *Utilize other healthcare professionals to help*
- Reimbursement for time
  - *Some billing options available (Medication Therapy Management (MTM); billing codes for general wellness visit)*
- Insufficient information from patient
  - *Utilize other healthcare professionals to help*
- Inappropriate setting: Reluctance to alter treatment not related to patient encounter/visit
  - *Communicate recommendations to provider and follow up*
- Multiple providers/specialists
  - *Don’t assume other providers are resistant to changes/deprescribing and communicate concerns*

PHARMACIST'S ROLE IN DEPRESCRIBING

- Community Setting
  - *Comprehensive medication management*
  - *Detect drug-drug interactions*
  - *Selection of appropriate OTC medications*
  - *Suggest specific dose adjustments or tapering schedules to provider*
  - *Help reduce medication costs by suggesting therapeutic alternatives*
  - *Counsel patient/caregiver to monitor for symptoms*
- Long-Term Care Setting
  - *Review all medications, labs, vitals, nurse and physician notes, patient concerns*
  - *Communicate specific suggestions with prescriber, nursing staff, and medical director*
  - *Make suggestions for monitoring*
  - *Follow up at next review*
  - *Maintain compliance for Centers for Medicare and Medicaid Services (CMS)*

PHARMACIST'S ROLE IN DEPRESCRIBING

- Hospital Setting
  - *Medication reconciliation*
  - *First-dose review on all new medication orders*
  - *Discontinue medications added during hospitalization at discharge if no longer needed*
  - *Communicate recommendations for deprescribing to primary care physician to review at post-hospitalization visit*
  - *Bedside delivery for discharge*
- Clinic Setting
  - *Medication reconciliation*
  - *First-dose review on all new medication orders*
  - *Monitor labs such as INRs, HgA1c, lipid panels and make dose adjustments*
  - *Follow up with patient*

TRANSITIONS IN CARE: PATIENTS NEARING THE END OF LIFE

- Goals shift to improving quality of life over prolonging life
- Carefully weight benefits vs. risks for each medication
- Less time to benefit from preventive medication therapy
  - *Cholesterol-lowering medications*
  - *Osteoporosis therapies*
- Some medications commonly avoided in elderly may be of benefit in palliative or hospice care settings
  - *Benzodiazepines*
  - *Anticholinergics*
  - *Opioids*

ONGOING PROCESS

Deprescribing takes time. Trials fail. Goals change. Benefits and risks should constantly be weighed.

Question 1

- Which of the following describe normal physiologic changes that occur in the aging body?
  A. *Liver mass increases*
  B. *Motility of the large intestine increases*
  C. *Kidney blood flow decreases*
  D. *Both A and C*
  E. *All of the above*

Question 1

- Which of the following describe normal physiologic changes that occur in the aging body?
  - *A. Liver mass increases*
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  - *C. Kidney blood flow decreases*
  - *D. Both A and C*
  - *E. All of the above*

Question 2

- Which medication requires dosage adjustment for renal impairment?
  A. *Nitrofurantoin*
  B. *Levetiracetam*
  C. *Gabapentin*
  D. *All of the above*

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- Which medication requires dosage adjustment for renal impairment?
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Question 3

- What are the potential benefits of deprescribing medications?
  A. *Reduce medication burden*
  B. *Prevent falls*
  C. *Reduce risk of hospitalization*
  D. *Improve cognitive function*
  E. *All of the above*

Question 3

- What are the potential benefits of deprescribing medications?
  - A. *Reduce medication burden*
  - B. *Prevent falls*
  - C. *Reduce risk of hospitalization*
  - D. *Improve cognitive function*
  - E. *All of the above*

Any other questions?

References

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