

# Pharmacology Knowledge Base

## Pharmacokinetics and Pharmacodynamics

### Pharmacokinetics (ADME)

- **Absorption**: Drug uptake from administration site
- Bioavailability: Fraction reaching systemic circulation
- First-pass metabolism: Hepatic metabolism before systemic circulation
- Routes: Oral, IV, IM, SC, topical, inhalation
- **Distribution**: Drug movement throughout body
- Volume of distribution (Vd): Apparent volume drug distributes into
- Protein binding: Albumin, alpha-1-acid glycoprotein
- Blood-brain barrier: Lipophilic drugs cross more easily
- **Metabolism**: Drug biotransformation
- Phase I: Oxidation, reduction, hydrolysis (CYP450 enzymes)
- Phase II: Conjugation reactions (glucuronidation, sulfation)
- Hepatic clearance: Liver's ability to eliminate drug
- **Excretion**: Drug elimination from body
- Renal clearance: Glomerular filtration, tubular secretion/reabsorption
- Half-life: Time for drug concentration to decrease by 50%
- Steady state: Achieved after 5 half-lives

### Pharmacodynamics

- **Receptor Theory**: Drug-receptor interactions
- **Dose-Response Relationships**: ED50, therapeutic window
- **Agonists**: Activate receptors (full, partial)
- **Antagonists**: Block receptors (competitive, non-competitive)
- **Tolerance**: Decreased response with repeated exposure
- **Dependence**: Physical/psychological need for drug

## Cardiovascular Pharmacology

### Antihypertensive Agents

- **ACE Inhibitors**: Lisinopril, enalapril
- Mechanism: Block angiotensin-converting enzyme
- Side effects: Dry cough, hyperkalemia, angioedema

- Contraindications: Pregnancy, bilateral renal artery stenosis
- **ARBs**: Losartan, valsartan
- Mechanism: Block angiotensin II receptors
- Advantages: No cough, similar efficacy to ACE inhibitors
- **Calcium Channel Blockers**: Amlodipine, diltiazem, verapamil
- Dihydropyridines: Peripheral vasodilation
- Non-dihydropyridines: Cardiac effects, AV node blockade
- **Beta-blockers**: Metoprolol, atenolol, propranolol
- Selective ( $\beta_1$ ): Cardiosensitive
- Non-selective ( $\beta_1/\beta_2$ ): Bronchospasm risk
- Contraindications: Asthma, severe heart failure

## Anticoagulants and Antiplatelets

- **Warfarin**: Vitamin K antagonist
- Monitoring: INR (International Normalized Ratio)
- Reversal: Vitamin K, fresh frozen plasma, prothrombin complex concentrate
- Drug interactions: CYP2C9, VKORC1 polymorphisms
- **Heparin**: Activates antithrombin III
- Unfractionated: IV, monitored by aPTT
- Low molecular weight: SC, predictable dosing
- Reversal: Protamine sulfate
- **DOACs**: Direct oral anticoagulants
- Dabigatran: Direct thrombin inhibitor
- Rivaroxaban, apixaban: Factor Xa inhibitors
- Advantages: Fixed dosing, fewer interactions
- **Antiplatelets**: Aspirin, clopidogrel, ticagrelor
- Aspirin: Irreversible COX-1 inhibition
- P2Y<sub>12</sub> inhibitors: ADP receptor blockade
- Dual antiplatelet therapy: Post-PCI, ACS

## Central Nervous System Pharmacology

### Antidepressants

- **SSRIs**: Sertraline, fluoxetine, escitalopram
- Mechanism: Selective serotonin reuptake inhibition
- Side effects: GI upset, sexual dysfunction, serotonin syndrome
- Discontinuation: Gradual taper to avoid withdrawal
- **SNRIs**: Venlafaxine, duloxetine

- Mechanism: Serotonin and norepinephrine reuptake inhibition
- Indications: Depression, anxiety, neuropathic pain
- **Tricyclics**: Amitriptyline, nortriptyline
- Mechanism: Multiple neurotransmitter reuptake inhibition
- Side effects: Anticholinergic, sedation, cardiac toxicity
- Overdose: QRS widening, sodium bicarbonate treatment

## Antiepileptics

- **Phenytoin**: Sodium channel blocker
- Monitoring: Serum levels, CBC, liver function
- Side effects: Gingival hyperplasia, hirsutism, ataxia
- Zero-order kinetics: Small dose changes cause large level changes
- **Carbamazepine**: Sodium channel blocker
- Indications: Focal seizures, trigeminal neuralgia
- Side effects: Diplopia, ataxia, hyponatremia
- Drug interactions: CYP3A4 inducer
- **Valproic Acid**: Multiple mechanisms
- Broad spectrum: Generalized and focal seizures
- Side effects: Weight gain, hair loss, teratogenicity
- Monitoring: Liver function, platelet count

## Opioid Analgesics

- **Morphine**: Gold standard opioid
- Metabolism: Glucuronidation, active metabolites
- Side effects: Respiratory depression, constipation, tolerance
- **Fentanyl**: Synthetic opioid, high potency
- Routes: IV, transdermal, sublingual
- Rapid onset, short duration
- **Oxycodone**: Semi-synthetic, oral bioavailability
- **Tramadol**: Weak opioid, serotonin/norepinephrine reuptake inhibition

## Antimicrobial Pharmacology

### Beta-lactam Antibiotics

- **Penicillins**: Penicillin G, amoxicillin, piperacillin
- Mechanism: Cell wall synthesis inhibition
- Resistance: Beta-lactamase production

- Allergies: Cross-reactivity with cephalosporins (low)
- **Cephalosporins**: Cephalexin, ceftriaxone, ceftaroline
- Generations: 1st (gram-positive) to 5th (MRSA)
- Side effects: GI upset, C. difficile colitis
- **Carbapenems**: Imipenem, meropenem, ertapenem
- Broad spectrum: Gram-positive, gram-negative, anaerobes
- Reserved for severe infections, carbapenem resistance

## Fluoroquinolones

- **Ciprofloxacin, Levofloxacin**: DNA gyrase inhibition
- **Spectrum**: Gram-negative, atypical organisms
- **Side effects**: Tendon rupture, QT prolongation, C. difficile
- **Resistance**: Increasing, especially in gram-negatives

## Macrolides

- **Azithromycin, Clarithromycin**: Protein synthesis inhibition
- **Spectrum**: Gram-positive, atypicals (Mycoplasma, Chlamydia)
- **Side effects**: GI upset, QT prolongation
- **Drug interactions**: CYP3A4 inhibition (clarithromycin)

# Endocrine Pharmacology

## Diabetes Medications

- **Insulin**: Rapid, short, intermediate, long-acting
- Types: Regular, NPH, glargine, detemir, degludec
- Routes: SC, IV (regular insulin only)
- Side effects: Hypoglycemia, weight gain, lipodystrophy
- **Metformin**: Biguanide, first-line type 2 diabetes
- Mechanism: Decreased hepatic glucose production
- Side effects: GI upset, lactic acidosis (rare)
- Contraindications: Renal impairment, contrast exposure
- **Sulfonylureas**: Glyburide, glipizide
- Mechanism: Insulin secretion stimulation
- Side effects: Hypoglycemia, weight gain
- **SGLT2 Inhibitors**: Empagliflozin, canagliflozin
- Mechanism: Glucose reabsorption inhibition
- Benefits: Weight loss, cardiovascular protection

- Side effects: UTIs, DKA, amputation risk

## Thyroid Medications

- **Levothyroxine**: Synthetic T4, hypothyroidism treatment
- Dosing: Weight-based, TSH monitoring
- Interactions: Iron, calcium, coffee affect absorption
- **Methimazole**: Antithyroid, hyperthyroidism treatment
- Mechanism: Thyroid hormone synthesis inhibition
- Side effects: Agranulocytosis, hepatotoxicity

## Drug Interactions and Safety

### Cytochrome P450 System

- **Major Enzymes**: CYP3A4, CYP2D6, CYP2C9, CYP2C19
- **Inducers**: Phenytoin, carbamazepine, rifampin
- **Inhibitors**: Ketoconazole, erythromycin, grapefruit juice
- **Clinical Significance**: Altered drug levels, efficacy, toxicity

### Adverse Drug Reactions

- **Type A**: Dose-dependent, predictable (80% of ADRs)
- **Type B**: Dose-independent, unpredictable (allergic reactions)
- **Monitoring**: Therapeutic drug monitoring, laboratory values
- **Reporting**: FDA MedWatch, pharmacovigilance

### Special Populations

- **Pediatric**: Weight-based dosing, developmental considerations
- **Geriatric**: Polypharmacy, altered pharmacokinetics
- **Pregnancy**: FDA categories, teratogenicity risk
- **Renal Impairment**: Dose adjustments, nephrotoxicity
- **Hepatic Impairment**: Metabolism alterations, hepatotoxicity