CHAPTER 8

MAJOR DRUG CLASSES I

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Abstract

Major drug classes involving cardiovascular, respiratory, gastrointestinal, and endocrine conditions represent cornerstone therapies for prevalent chronic diseases. Cardiovascular medications comprises of antihypertensives acting through distinct mechanisms (ACE inhibitors, ARBs, calcium channel blockers, diuretics, beta-blockers), antiarrhythmics classified by electrophysiologic effects, lipid-lowering agents including statins and newer targeted therapies, anticoagulants spanning vitamin K antagonists and direct oral agents, and heart failure medications including beta-blockers, sacubitril/valsartan, and SGLT2 inhibitors demonstrating mortality benefits. Respiratory drugs target bronchospasm through beta-agonists with varying onset and duration profiles; reduce inflammation through inhaled corticosteroids and biological agents targeting specific inflammatory pathways; address allergic responses with antihistamines, leukotriene modifiers, and mast cell stabilizers; and treat pulmonary infections with diverse antimicrobial classes, each requiring specific administration techniques and monitoring parameters. Gastrointestinal agents include acid-suppressing medications (proton pump inhibitors, H2-antagonists), antiemetics targeting central and peripheral pathways, laxatives with mechanical and stimulant mechanisms, antidiarrheals, pancreatic enzymes, and newer biologics for inflammatory bowel disease targeting specific immune pathways. Endocrine medications consist of diabetes therapies including insulins with distinct pharmacokinetic profiles, oral agents with varied mechanisms, and newer injectable therapies; thyroid replacements requiring narrow therapeutic monitoring; reproductive hormones used in contraception and hormone replacement; and osteoporosis treatments spanning bisphosphonates, RANK ligand inhibitors, and anabolic agents, each with specific administration requirements and monitoring needs.

Keywords: *Chronic Disease; Mechanism of Action; Therapeutic Selection; Drug Administration; Monitoring Parameters*

Learning Objectives

After completion of the chapter, the learners should be able to:

- Compare and contrast the mechanisms of action, indications, contraindications, and monitoring parameters for major classes of cardiovascular medications.
- Select appropriate respiratory medications based on specific airway disease pathophysiology, patient factors, and device considerations.
- Recommend appropriate gastrointestinal agents for specific conditions based on mechanism of action, onset of effect, and adverse effect profiles.
- Design monitoring plans for patients on endocrine therapies that address both efficacy markers and potential adverse effects.
- Develop patient education strategies for complex medication regimens used in chronic disease management.
- Identify and manage clinically significant drug interactions associated with common cardiovascular, respiratory, gastrointestinal, and endocrine medications.

CARDIOVASCULAR SYSTEM

Cardiovascular medications constitute a cornerstone of modern pharmacotherapy, addressing the leading causes of morbidity and mortality worldwide. These agents target multiple physiological pathways to manage hypertension, dyslipidemia, thrombotic disorders, heart failure, and arrhythmias. Treatment approaches typically involve combination therapy addressing different pathophysiological mechanisms to achieve optimal outcomes. The pharmacist's role extends beyond dispensing to include monitoring therapeutic efficacy, identifying adverse effects, ensuring medication adherence, and facilitating appropriate lifestyle modifications that complement pharmacological interventions.

Antihypertensive Agents

Hypertension management employs several complementary drug classes targeting different mechanisms of blood pressure regulation. Thiazide diuretics reduce blood pressure through modest sodium and water excretion, with subsequent vasodilation from decreased peripheral vascular resistance. These agents remain first-line therapy for many patients due to their efficacy, safety profile, and cost-effectiveness, though electrolyte abnormalities necessitate periodic monitoring. Angiotensin-converting enzyme inhibitors (ACEIs) prevent the formation of angiotensin II, reducing vasoconstriction and aldosterone

release while potentially offering cardiorenal protective effects independent of blood pressure reduction.

Table 8.1: Antihypertensive Medications

Drug Class	Examples	Mechanism of Action
ACE Inhibitors	Lisinopril Enalapril Ramipril	Block angiotensin II production
ARBs	Losartan Valsartan Candesartan	Block angiotensin II receptors
Calcium Channel Blockers (Dihydropyridines)	Amlodipine Nifedipine Felodipine	Block calcium entry into vascular smooth muscle
Calcium Channel Blockers (Non-dihydropyridines)	Diltiazem Verapamil	Block calcium entry into cardiac cells
Thiazide Diuretics	Hydrochlorothiazide Chlorthalidone Indapamide	Inhibit Na+/Cl- reabsorption in distal tubule
Loop Diuretics	Furosemide Bumetanide Torsemide	Inhibit Na+/K+/2Cl- reabsorption in loop of Henle
Potassium-Sparing Diuretics	Spironolactone Eplerenone Amiloride	Block aldosterone or ENaC
Beta Blockers	Metoprolol Carvedilol Bisoprolol	Block beta-adrenergic receptors
Alpha Blockers	Doxazosin Terazosin Prazosin	Block alpha-adrenergic receptors
Central Alpha-2 Agonists	Clonidine Methyldopa	Stimulate central alpha-2 receptors
Direct Vasodilators	Hydralazine Minoxidil	Relax vascular smooth muscle
Direct Renin Inhibitors	Aliskiren	Inhibit renin activity

The characteristic dry cough results from bradykinin accumulation and may necessitate transition to angiotensin II receptor blockers (ARBs), which provide similar benefits without affecting bradykinin metabolism. Calcium channel blockers induce vasodilation through inhibition of calcium influx into vascular smooth muscle cells, with dihydropyridines (e.g., amlodipine) demonstrating greater vascular selectivity compared to non-dihydropyridines (e.g., diltiazem, verapamil), which exert additional effects on cardiac conduction. Beta-adrenergic blockers reduce cardiac output and renin release, with newer vasodilatory agents offering more favorable metabolic profiles than traditional non-selective compounds.

Lipid-Modifying Medications

Dyslipidemia management focuses primarily on reducing atherosclerotic cardiovascular risk through targeting specific lipid fractions. Statins (HMG-CoA reductase inhibitors) remain the foundation of therapy, reducing low-density lipoprotein cholesterol (LDL-C) through inhibition of hepatic cholesterol synthesis and upregulation of LDL receptors. The demonstrated mortality benefit extends beyond lipid effects to include plaque stabilization and anti-inflammatory properties. Myalgias represent the most common adverse effect, with true myopathy and rhabdomyolysis occurring rarely but requiring vigilant monitoring. Ezetimibe selectively inhibits intestinal cholesterol absorption, providing modest LDL-C reduction as monotherapy but substantial additive effects when combined with statins. PCSK9 inhibitors, administered as subcutaneous injections, dramatically reduce LDL-C by preventing degradation of LDL receptors, offering therapeutic options for patients with familial hypercholesterolemia or statin intolerance. Fibrates primarily reduce triglycerides and modestly increase high-density lipoprotein cholesterol (HDL-C) through activation of peroxisome proliferator-activated receptor-alpha (PPAR-α), though their role has diminished with evidence suggesting limited cardiovascular outcome benefits beyond statin therapy.

Anticoagulants and Antiplatelets

Thrombotic disorder management employs agents targeting the coagulation cascade or platelet function. Traditional anticoagulation with warfarin inhibits vitamin K-dependent clotting factors (II, VII, IX, X), requiring close monitoring through International Normalized Ratio (INR) testing due to numerous food and drug interactions affecting its metabolism. Direct oral anticoagulants (DOACs) offer targeted inhibition of specific coagulation factors—either thrombin (dabigatran) or factor Xa (rivaroxaban, apixaban, edoxaban)—with predictable

pharmacokinetics enabling fixed dosing without routine monitoring. However, renal function assessment remains essential for appropriate dose selection. Antiplatelet agents prevent thrombotic events through various mechanisms: aspirin irreversibly inhibits cyclooxygenase-1 (COX-1), reducing thromboxane A2 production; P2Y12 inhibitors (clopidogrel, prasugrel, ticagrelor) prevent ADP-mediated platelet activation; and glycoprotein IIb/IIIa inhibitors block the final common pathway of platelet aggregation in acute coronary syndromes. Dual antiplatelet therapy balances enhanced antithrombotic efficacy against increased bleeding risk, with duration tailored to specific clinical scenarios.

Heart Failure Medications

Heart failure pharmacotherapy aims to reduce symptoms, improve quality of life, and decrease mortality through targeting neurohormonal activation and hemodynamic derangements. Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) counteract the detrimental effects of renin-angiotensin-aldosterone system activation, reducing afterload and preventing pathologic remodeling. Beta-adrenergic blockers, once contraindicated in heart failure, now represent foundational therapy through attenuation of sympathetic nervous system hyperactivation, with carvedilol, metoprolol succinate, and bisoprolol demonstrating mortality benefits in landmark trials. Mineralocorticoid receptor antagonists (spironolactone, eplerenone) provide additional neurohormonal modulation while reducing potassium wasting, though hyperkalemia risk necessitates careful monitoring, particularly when combined with ACEIs or ARBs. The angiotensin receptor-neprilysin inhibitor sacubitril/valsartan represents a therapeutic advancement by simultaneously blocking angiotensin II effects while preventing degradation of beneficial natriuretic peptides. Loop diuretics manage congestion without mortality benefit, requiring careful dose titration to balance symptom relief against electrolyte disturbances and renal dysfunction. Sodium-glucose cotransporter-2 (SGLT2) inhibitors have emerged as a novel therapeutic class with demonstrated benefits in heart failure with reduced ejection fraction, even in non-diabetic patients, potentially through multiple mechanisms including improved cardiac energetics and reduced cardiac preload.

Table 8.2: Cardiovascular Medications

Drug Class	Examples	Mechanism of Action
HMG-CoA Reductase Inhibitors (Statins)	Atorvastatin Rosuvastatin Simvastatin	Inhibit cholesterol synthesis
PCSK9 Inhibitors	Alirocumab Evolocumab	Decrease LDL receptor degradation
Bile Acid Sequestrants	Cholestyramine Colesevelam	Bind bile acids in intestine
Fibric Acid Derivatives	Fenofibrate Gemfibrozil	Activate PPAR-α
Niacin	Niacin/Nicotinic acid	Multiple lipid effects
Cardiac Glycosides	Digoxin	Inhibit Na+/K+ ATPase
Antiarrhythmics Class I	Flecainide Propafenone Procainamide	Sodium channel blockers
Antiarrhythmics Class III	Amiodarone Sotalol Dofetilide	Potassium channel blockers
Antiplatelet Agents	Aspirin Clopidogrel Ticagrelor	Inhibit platelet aggregation
Anticoagulants - Vitamin K Antagonists	Warfarin	Inhibit vitamin K-dependent clotting factors
Anticoagulants - Direct Oral	Apixaban Rivaroxaban Dabigatran	Target specific clotting factors
Nitrates	Nitroglycerin Isosorbide mononitrate	Increase nitric oxide, vasodilation
Inotropes	Milrinone Dobutamine	Increase cardiac contractility

RESPIRATORY SYSTEM

Respiratory pharmacotherapy addresses both acute and chronic conditions affecting the airways and lung parenchyma. These medications target bronchoconstriction, inflammation, mucus hypersecretion, and infectious processes to restore respiratory function and improve quality of life. Delivery methods significantly influence therapeutic efficacy, with inhalation routes providing direct delivery to the target tissues while minimizing systemic exposure. Proper inhaler technique remains critical for therapeutic success, necessitating thorough patient education and periodic reassessment by pharmacists.

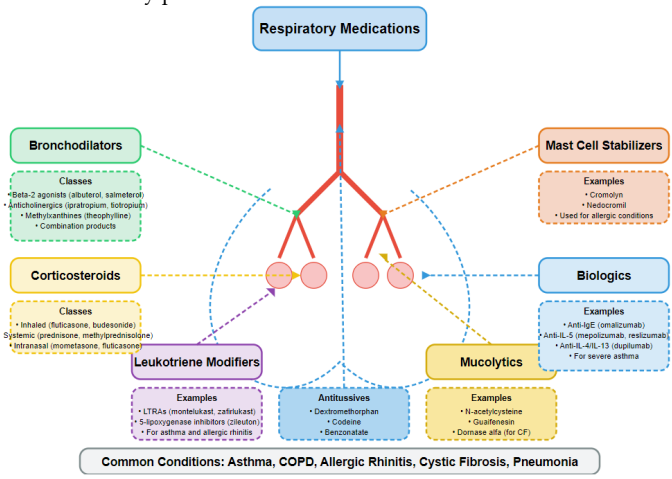

Figure 8.1: Drugs acting on Respiratory System

Bronchodilators

Bronchodilators relieve airflow limitation through relaxation of airway smooth muscle via different mechanisms. Beta2-adrenergic agonists stimulate adenylyl cyclase, increasing intracellular cyclic adenosine monophosphate (cAMP) and producing bronchodilation. Short-acting agents (salbutamol, terbutaline) provide rapid symptom relief within minutes but with brief duration, serving primarily as rescue medication. Long-acting formulations (salmeterol, formoterol, indacaterol) maintain bronchodilation over 12-24 hours, supporting maintenance therapy in asthma and chronic obstructive pulmonary disease (COPD). Potential adverse effects include tremor, tachycardia, and hypokalemia, particularly with excessive use. Anticholinergic

bronchodilators block muscarinic receptors, inhibiting acetylcholine-mediated bronchoconstriction. Short-acting compounds (ipratropium) demonstrate efficacy primarily in COPD, while long-acting agents (tiotropium, umeclidinium, glycopyrronium) provide sustained bronchodilation with once-daily dosing and potential reduction in exacerbation frequency. Dry mouth represents the most common adverse effect, with urinary retention and glaucoma exacerbation occurring rarely. Methylxanthines (theophylline) offer modest bronchodilation through phosphodiesterase inhibition and adenosine antagonism, but their narrow therapeutic index and numerous drug interactions have relegated them to third-line therapy in contemporary practice.

Anti-inflammatory Respiratory Medications

Airway inflammation represents a central pathophysiological feature in chronic respiratory diseases, necessitating targeted anti-inflammatory therapy. Inhaled corticosteroids (ICS) reduce airway inflammation through multiple mechanisms, including inhibition of inflammatory cytokine production, reduction of inflammatory cell recruitment, and downregulation of inflammatory mediators.

Table 8.3: Drugs acting on Respiratory System

Drug Class	Generic Examples	Mechanism of Action	Indications
Short-Acting Beta-2 Agonists (SABAs)	Albuterol Levalbuterol	Stimulate beta-2 receptors in airways	Acute bronchospasm Exercise-induced bronchospasm
Long-Acting Beta-2 Agonists (LABAs)	Salmeterol Formoterol Olodaterol	Stimulate beta-2 receptors with extended duration	Asthma (with ICS) COPD maintenance
Short-Acting Muscarinic Antagonists (SAMAs)	Ipratropium	Block muscarinic receptors in airways	COPD Asthma exacerbations