Only the **unbound fraction** of many drugs is readily filtered at the glomerulus.

2. Tubular secretion

Some drugs are actively transported from the blood into the renal tubules.

3. Tubular reabsorption

Some drugs can move from the renal tubules back into the bloodstream.

The degree of reabsorption can be influenced by factors such as:

- Lipid solubility
- Degree of ionization
- Urinary pH

🧹 DRUG CLEARANCE

Clearance (CL) describes the volume of plasma from which a drug is completely removed per unit of time.

Total body clearance represents the combined contribution of different organs.

Main contributors

- Renal clearance
- Hepatic clearance
- Other routes of elimination

🧠 Remember

Clearance = how efficiently the body removes a drug from plasma.

📝 QUICK SELF-TEST

1. What does bioavailability describe?
The fraction of an administered dose that reaches systemic circulation unchanged.

2. Which route provides 100% bioavailability?
Intravenous administration.

3. What is first-pass metabolism?
Metabolism of an orally absorbed drug before it reaches systemic circulation.

4. What are the three major Phase I reactions?
Oxidation, reduction, and hydrolysis.

5. What are Phase II reactions mainly called?
Conjugation reactions.

6. Which organ is the major site of drug metabolism?

Like other β-lactams, these drugs bind to PBPs and inhibit bacterial cell-wall synthesis.

A major distinguishing feature is activity against certain resistant Gram-positive organisms.

⭐ Key point

Ceftaroline is active against MRSA because it can bind the altered PBP associated with methicillin resistance.

Ceftaroline → β-lactam + MRSA coverage

🩺 Indications

Ceftaroline is used for susceptible infections including:

- Community-acquired bacterial pneumonia
- Acute bacterial skin and skin-structure infections

Ceftobiprole, where approved, has additional uses depending on local guidelines and regulatory indications.

🚫 Contraindications / Important precautions

- Severe hypersensitivity to the drug or relevant β-lactam antibiotics
- Caution in patients with a history of serious β-lactam allergy
- Renal function should be assessed because dosing may need adjustment in renal impairment.

Side effects

Possible adverse effects include:

- Nausea
- Diarrhea
- Rash
- Headache
- Injection-site reactions
- Hypersensitivity reactions
- C. difficile-associated diarrhea

Rare but important:

- **Neutropenia**, particularly with prolonged therapy

👩🏽‍⚕️ Nursing considerations

- Check allergy history before administration.
- Obtain cultures when appropriate.
- Monitor temperature and clinical response.
- Monitor CBC when prolonged treatment makes this clinically appropriate.
- Monitor renal function.

Drug	Main target	Main use	Key feature
Eszopiclone	GABA-A receptor complex	Insomnia	Sedative-hypnotic
Zolpidem	GABA-A receptor complex	Insomnia	Rapid sleep-promoting effect
Ramelteon	MT_1/MT_2 receptors	Sleep-onset insomnia	Mimics melatonin activity

🍺 PHARMACOLOGICAL MANAGEMENT OF ALCOHOL DEPENDENCE

Treatment of alcohol dependence may involve **medications together with psychosocial support**. Medication choice depends on the patient's clinical situation.

NALTREXONE

Drug class

Opioid receptor antagonist

Mechanism of action

Naltrexone blocks **opioid receptors**, reducing the rewarding effects associated with alcohol consumption and helping decrease alcohol craving in appropriate patients.

Forms

- Oral formulation
- Long-acting injectable formulation

Therapeutic use

- Maintenance treatment for **alcohol-use disorder** as part of a comprehensive treatment programme.

Important point

Naltrexone **does not produce the alcohol withdrawal reaction** and is not used to manage acute alcohol withdrawal symptoms.

Nursing considerations

- Assess the patient's alcohol-use history.
- Check for current opioid use before administration.

1.CHOLINOMIMETIC DRUGS & CHOLINESTERASE INHIBITORS

What Are Cholinomimetic Drugs?

Cholinomimetic drugs, also called **parasympathomimetics or cholinergic drugs**, are agents that **mimic the effects of acetylcholine (ACh)**.

In contrast:

Parasympatholytic / anticholinergic drugs oppose the effects produced by parasympathetic stimulation.

Major cholinergic receptors

Acetylcholine acts through:

- **Muscarinic receptors:** M_1, M_2, M_3, M_4 and M_5
- **Nicotinic receptors:** neuronal and neuromuscular types

Classification of Cholinomimetic Drugs

Cholinomimetics can be divided into:

A. Direct-acting agents

These interact directly with **cholinergic receptors**, thereby increasing cholinergic activity.

Choline esters

- Acetylcholine
- Carbachol
- Bethanechol
- Methacholine

Alkaloids

- Cevimeline
- Pilocarpine
- Arecoline
- Muscarine

B. Indirect-acting agents

These increase the availability of naturally produced ACh by **inhibiting acetylcholinesterase**.

They are divided into:

Reversible inhibitors

- Ambenonium

↑ intracellular Ca^{2+}
↓
↑ Force of cardiac contraction

A. 💊 Digoxin

Pharmacokinetics

- Oral bioavailability varies with the preparation.
- It has a relatively long half-life.
- It is mainly eliminated through the **urine**.
- Renal impairment can therefore increase the risk of accumulation.

⚠️ Toxicity

Digoxin has a **narrow therapeutic range**.

Toxicity may produce:

Gastrointestinal effects

- Nausea
- Vomiting
- Loss of appetite
- Diarrhea

Cardiac effects

- Bradycardia
- Cardiac arrhythmias

Factors increasing toxicity

- **Hypokalemia**
- Renal impairment
- Drug interactions

Management of Digoxin Toxicity

- Correct electrolyte abnormalities where appropriate.
- Severe toxicity may be treated with **digoxin-specific antibody fragments (Fab)**.
- Lidocaine or amiodarone may be used for certain serious ventricular arrhythmias depending on the clinical situation.

B. Phosphodiesterase Inhibitors

Examples:

- Milrinone
- Inamrinone

Action

Phosphodiesterase inhibition increases intracellular **cAMP**, producing:

- Increased cardiac contractility
- Vasodilation

C. β-Adrenergic Agonists

Examples:

- Dopamine
- Dobutamine
- Isoproterenol

These agents stimulate β-adrenergic receptors and increase cardiac activity.

Dopamine may be used in selected patients with severe circulatory compromise, including cardiogenic shock.

💧 B. Drugs WITHOUT a Primary Positive Inotropic Effect

1. Diuretics

High-efficacy loop diuretics

- Furosemide
- Bumetanide

Thiazide/thiazide-related diuretics

- Hydrochlorothiazide
- Metolazone

Potassium-sparing diuretics

- Spironolactone
- Triamterene

Main action

↑ Sodium and water excretion

→ ↓ Fluid accumulation
→ ↓ Circulatory volume
→ Relief of congestion

2. ACE INHIBITORS

Examples:

Nicotinic acid	Niacin

💊 A. STATINS

Examples

- Atorvastatin
- Simvastatin
- Rosuvastatin
- Pravastatin

⚙️ Mechanism of Action

Statins inhibit:

HMG-CoA reductase

→ ↓ Hepatic cholesterol synthesis
→ ↑ Hepatic LDL receptors
→ ↑ Removal of LDL from blood
→ **↓ LDL cholesterol**

Therapeutic Uses

- Hypercholesterolemia
- Prevention of cardiovascular disease
- Reduction of cardiovascular events in high-risk patients

Adverse Effects

- Muscle pain
- Increased liver enzymes
- Rarely, **rhabdomyolysis**

Nursing Responsibilities

- Monitor lipid profile.
- Monitor liver function when clinically indicated.
- Ask about unexplained muscle pain or weakness.
- Review potential drug interactions.
- Reinforce dietary and lifestyle measures.

💊 B. FIBRATES

Examples

These symptoms become worse at night.

STATUS ASTHMATICUS

Status asthmaticus refers to severe acute asthma.

It is a **life-threatening condition** associated with:

- Exhaustion
- Cyanosis
- Bradycardia
- Hypotension
- Dehydration
- Metabolic acidosis

CARDIAC ASTHMA

Cardiac asthma is **bronchospasm precipitated by uncompensated congestive heart failure**.

PATHOPHYSIOLOGY OF ASTHMA

Antigens such as **pollen and house-dust mites** can sensitize susceptible patients.

They stimulate production of **IgE antibodies**.

The IgE antibodies may:

- Remain circulating in the blood, or
- Become attached to mast cells in nasal or bronchial tissues and to basophils.

On re-exposure to the same antigen

An antigen-antibody reaction occurs during the early phase.

This causes **degranulation of lung mast cells**, resulting in the release of powerful bronchoconstricting mediators.

These include:

- Histamine
- 5-HT
- PGD_2
- Cysteinyl leukotrienes:
  - LTB_4
  - LTC_4
  - LTD_4

Mast-cell cytokines

Lung mast cells also release:

The source gives a half-life of approximately:

12 hours

Onset and duration

- Effect begins after approximately **15–20 minutes**
- Duration is approximately **12 hours**

Examples

- Salmeterol
- Formoterol

β_2-agonists are available as **metered-dose aerosols**.

SELECTIVE β_2-ADRENOMIMETICS WITH Tocolytic Effect

The following β_2-adrenomimetics are listed as having a **tocolytic effect**:

- Fenoterol
  - Partusisten® — tablet 5 mg
- Hexoprenaline
- Salbutamol
  - Salbupart®
- Terbutaline
- Ritodrine

Tocolytics

Tocolytics **suppress premature labour**.

Non-selective β-agonists

- Epinephrine
- Isoprenaline
- Orciprenaline
- Ephedrine

M-cholinolytics

- Ipratropium
- Tiotropium
- Oxitropium

Methyl xanthines

- Theophylline
- Aminophylline
- Theotard

- PAF

These mediators normally contribute to:

- Increased vascular permeability
- Oedema
- Leukocyte migration
- Fibrin deposition

Overall effect

GCS suppress inflammation by inhibiting:

- Movement of fluid and protein into tissues
- Migration and function of neutrophils and eosinophils
- Histamine synthesis in mast cells
- Production of pro-inflammatory substances

Benefits

This results in:

- Decreased mucus secretion
- Decreased oedema
- Reduced reactivity

CORTICOSTEROIDS

- A second action of corticosteroids is to **increase the number and sensitivity of β_2-adrenergic receptors**.

Routes

- They can be administered:
  - PO
  - IV

Clinical response

- Pulmonary function usually improves within:
- **6–8 hours**
- Treatment is continued for:
- **7–10 days**

STEROIDS

Inhaled steroids

- Inhaled steroids have **fewer long-term side effects**.
- COPD

Allergic rhinitis may be:

- Seasonal
- Perennial

Possible consequences

It can lead to:

- Chronic fatigue
- Difficulty sleeping
- Sinus infections
- Postnasal drip
- Cough
- Headache

32. INTRANASAL DRUGS FOR ALLERGIC RHINITIS

Examples listed include:

- Atrovent nasal spray
- Beconase — beclomethasone
- Rhinocort — budesonide
- Flonase — fluticasone
- Nasonex — mometasone
- Nasalcrom — mast cell stabilizer

33. ALLERGIC CONTACT DERMATITIS

Allergic contact dermatitis is *a*:

Type IV hypersensitivity reaction

Example

Poison ivy

Timing

It usually occurs **more than 24 hours after re-exposure**.

34. OTHER ALLERGIC REACTIONS

Allergic food reactions

🏥 Therapeutic Uses

Used when the pancreas does not produce enough digestive enzymes, such as in:

- **Chronic pancreatitis**
- Cystic fibrosis
- Pancreatectomy
- Other causes of pancreatic exocrine insufficiency

Adverse Effects

- Abdominal discomfort
- Nausea
- Constipation
- Diarrhea
- Perianal irritation

High doses, particularly in patients with cystic fibrosis, have been associated with **fibrosing colonopathy**.

👩‍⚕️ Nursing Responsibilities

- Administer **with meals and snacks**.
- Do not crush or chew delayed-release preparations.
- Monitor stool characteristics and GI symptoms.
- Monitor nutritional status and body weight.
- Ensure adequate enzyme dosing with food.
- Educate the patient on correct administration.

⭐ Memory tip

Pancrelipase = "Replace what the pancreas cannot make."

2.Gall Stone Drugs

1. 🟢 URSODIOL

Other name

Ursodeoxycholic acid (UDCA)

Drug class

Bile acid

⚙️ Mechanism of Action

Ursodiol alters the composition of bile and:

- Reduces intestinal absorption of cholesterol

MYCOPHENOLATE MOFETIL — PHARMACOKINETICS & TOXICITY

Pharmacokinetics

- Orally absorbed.
- MPA and its glucuronidated metabolites are bound to plasma albumin.
- Eliminated through urine.

Adverse effects

- Nausea, vomiting and diarrhea.
- Abdominal pain.
- Leukopenia and anemia.
- Higher doses increase the risk of cytomegalovirus (CMV) infection.

Drug interaction: Antacids containing magnesium or aluminium and cholestyramine can reduce absorption.

7. IMMUNOSUPPRESSIVE ANTIBODIES

Immunosuppressive antibodies play a pivotal role in prolonging allograft survival.

Polyclonal antibodies: Produced by immunizing rabbits or horses with human lymphocyte antigens. They are relatively inexpensive but variable in composition.

Monoclonal antibodies: Produced using hybridoma or recombinant-DNA technology. They are homogeneous, specific and cost-effective.

ANTITHYMOCYTE GLOBULINS

Polyclonal antibodies directed against thymic/T-cell precursor populations.

Uses

- Used with other immunosuppressants at transplantation to prevent early allograft rejection.
- Treatment of severe rejection episodes.
- Treatment of corticosteroid-resistant acute rejection.
- Rabbit preparations are described as more potent than horse preparations.

Mechanism

Antibodies bind the surface of circulating T lymphocytes and promote complement-mediated destruction, antibody-dependent cytotoxicity, apoptosis and opsonization. The antibody-bound cells are phagocytosed in the liver and spleen, producing lymphopenia and impaired T-cell responses.

Pharmacokinetics: IV infusion; half-life about 3–9 days.

Adverse effects: chills and fever, leukopenia, thrombocytopenia, viral infections including CMV, and skin rashes. Antibodies may also develop against these foreign proteins.

Interaction	Effect
Calcium-channel blockers + vincristine	↑ vincristine effect
Digoxin	↓ digoxin effect
Dilantin/phenytoin	↓ phenytoin effect

🎯5 MAJOR ANTICANCER DRUGS TO KNOW

High-yield focus: know the mechanism, uses and toxicity of these drugs:

⭐ DOXORUBICIN

Class: Anthracycline antibiotic
Key concern: Cardiotoxicity

⭐ CISPLATIN

Class: Platinum-containing compound
Key toxicity: NON

- Nephrotoxicity
- Ototoxicity
- Neurotoxicity

⭐ CYCLOPHOSPHAMIDE

Class: Alkylating agent
Key toxicity: Hemorrhagic cystitis

⭐ METHOTREXATE

Class: Antimetabolite
Key concept: Folate antagonism + leucovorin rescue

⭐ VINCRISTINE

Class: Vinca alkaloid / antimitotic agent
Key concept: M-phase blockade

🧠 ANTICANCER DRUG CLASSIFICATION — MASTER TABLE

Class	Cell-cycle relationship	Examples
Alkylating agents	Non-specific	Cyclophosphamide, melphalan, chlorambucil
Platinum compounds	Discussed with alkylating agents	Cisplatin, carboplatin, oxaliplatin
Antimetabolites	**S-phase specific**	Methotrexate, 5-FU, cytarabine
Antimitotic agents	**M-phase**	Vinca alkaloids, paclitaxel
Topoisomerase I inhibitors	Cell-cycle related	Topotecan
Topoisomerase II inhibitors	Cell-cycle related	Teniposide
Cytotoxic antibiotics	Non-specific	Doxorubicin, bleomycin
Miscellaneous agents	Varies	Hydroxyurea, mitotane, retinoic acid derivatives
Targeted agents	Specific molecular targets	Listed as a separate category
Hormonal therapy	Hormone-dependent cancers	Anti-estrogens, progestins, GnRH analogs

🚨 EXTRAVASATION — IMPORTANT NURSING SECTION

Extravasation means leakage of a vesicant or irritating chemotherapy drug from the vein into surrounding tissue.

the material specifically emphasizes vesicant drugs .