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Textbook of Pharmacology *PHYGITAL*

Based on **INC Syllabus 2021-22**

III & IV Semesters

Textbook of Pharmacology

for BSc Nursing Students

As per the Revised INC Syllabus (2021–22) for BSc Nursing

PHARMACOLOGY

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3rd Edition

Joginder Singh Pathania
Rupendra Kumar Bharti
Vikas Sood

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Nursing Knowledge Tree
An Initiative by CBS Nursing Division

Third Edition

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CBS Nursing Knowledge Tree

Extends its Tribute to

Florence Nightingale

For glorifying the role of women as nurses,
For holding the title of " The Lady with the Lamp,"
For working tirelessly for humanity–
Florence Nightingale will always be
remembered for her
selfless and memorable services to the
human race.

Florence Nightingale
(May 1820 – August 1910)

ॐ सर्वे भवन्तु सुखिनः सर्वे सन्तु निरामयाः ।

सर्वे भद्रणिपश्यन्तु मा कश्चिद्दुःख भाग भवेत् ॥

Dedicated

to

Our Families, Teachers, Friends and Students

Preface to the Third Edition

We are immensely grateful for the overwhelming response and appreciation received for the first and second editions of *Textbook of Pharmacology for BSc Nursing Students*. The continued support, constructive feedback, and encouragement from students, educators, and professionals have been instrumental in shaping this third edition. It is with renewed commitment and passion that we present the updated and enriched third edition.

This edition has been thoughtfully revised to reflect the latest developments in pharmacology and to align with the current **Indian Nursing Council (INC) syllabus** guidelines. We remain steadfast in our objective—to make pharmacology simple, relevant, and practically applicable for nursing students. Whether it is understanding the intricate mechanisms of **pharmacokinetics and pharmacodynamics** or grasping the vital responsibilities of nurses in medication administration, this edition aims to bridge the gap between theory and clinical practice.

What's New in the Third Edition:

- **Updated Content as per the latest INC syllabus** ensuring the curriculum relevance and compliance with academic standards.
- **New Chapters and Topics** are added based on recent advancements, including drug updates related to emerging diseases, evolving treatment guidelines, and updated national drug policies.
- **Enhanced Clinical Case-based Learning** as each chapter begins with a realistic clinical scenario, followed by guided discussions and solutions to promote critical thinking and clinical correlation.
- **Expanded Nursing Implications** are provided as they are further refined into five well-structured sections—assessment, investigations, therapeutic goals, side effect management, and patient-centered care—for improved comprehension and clinical preparedness.
- **Additional Objective Questions and Case-based MCQs** are included to support examination readiness and conceptual clarity.
- **Errors from Previous Editions** are corrected and ambiguous areas are clarified for better accuracy and understanding.

We believe that this third edition will serve as a valuable companion for both students and educators who are learning and teaching pharmacology. It is our sincere hope that the updated structure, improved clarity, and enriched content will empower students to navigate this essential subject with confidence and competence.

We extend our heartfelt thanks to the readers who continue to place their trust in this book. Your feedback continues to inspire and guide us in our journey of academic excellence.

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Preface to the First Edition

Pharmacology is one of the basics as well as an applied medical sciences. It deals with the study of various drugs, their mode of action, pharmacological effects, side effects and drug-drug interactions. This subject is the backbone of all the drug treatments whatsoever are being used in medical practice as each and every medical specialty has to use drugs for the treatment of its patients. As, no treatment is complete without the use of drugs, appropriate knowledge of drugs is mandatory for all medical personnel involved in the use of drugs.

As we have been teaching Pharmacology to the students of Allied Health Sciences, like nurses or physiotherapists and students from other fields of Allied Health Sciences since long, we have seen the dilemma in the minds of these students about the appropriate book to follow. In a class, teacher sows the seeds of knowledge in the minds of students, but it is the book that provides water and manure to these seeds for sprouting and blooming into the flowers of knowledge. Hence, the idea of writing a pharmacology book erupted in our minds. This edition of the book is meant for the students of Allied Health Sciences as well as for other health professionals who are already working in the healthcare industry. As this book has been written and organized strictly according to the syllabus, it will be of immense help to the students all over India.

This book provides the basic concepts of Pharmacology in simple language with clinical correlations and adequate knowledge of the subject. The unnecessary theoretical details have been ignored. This book includes the recent drugs and latest concepts, which have been specially highlighted.

This book has been designed to provide a comprehensive, authoritative, simplified and precise knowledge of the subject. Most of the illustrations have been presented in the easily understandable tabular forms, figures and are properly highlighted for the ease of the students.

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Acknowledgments

Thanks to **The Almighty God**, Who provided us the strength and determination to accomplish the work of writing this book.

It is our proud privilege to express deep sense of gratitude and indebtness to **Dr AK Sahai** (Professor and Head), **Dr DD Gupta** (Professor) and **Dr PK Kaundal** (Professor) Department of Pharmacology, IGMC, Shimla, Himachal Pradesh, for their encouragement, constant supervision and able guidance.

We are sincerely thankful to **Dr Ritu Shitak** (Associate Professor), **Dr Anamika Thakur** (Assistant Professor) Department of Pharmacology and **Dr Yogesh Diwan** (Assistant Professor) and **Dr Kunal Chawla** (Assistant Professor) Department of Anatomy for their positive attitude and valuable suggestions during this project.

We are also thankful to the Senior Residents **(Dr Ramesh, Dr Meenakshi, Dr Aanchal)** and the Junior Residents **(Dr Navdha Sharma, Dr Sandeep Kaushik, Dr Vivek Thakur, Dr Sushma Sharma)** Department of Pharmacology for their support and sincere cooperation for completion of this book.

Dr Pratima Koshewara, MBBS, MS (Obstetrics & Gynecology), has authored Chapter 12: "Drugs Used for Hormonal Disorders and Supplementation, Contraception, and Medical Termination of Pregnancy" and Chapter 13: "Drugs Used for Pregnant Women During Antenatal, Labor, and Postnatal Period".

We cannot forget the cooperation we got from **Mr Rajan Bhimta**, **Mr Vijay Thakur**, **Ms Aditi**, **Ms Nalini** and all other staff members of the Department of Pharmacology, IGMC, Shimla.

We are sincerely thankful to **Ms Sampatti** for her sincere cooperation, constant encouragement and able guidance during the work.

I, **Dr JS Pathania**, express my profound gratitude to my parents, my wife **Dr Neelam Pathania**, **Siddharth Pathania** (loving son) and all family members for their patience, unfailing support and cooperation throughout this work period. Without their support and encouragement, this book could not have seen the light of the day.

With immense pride and deep gratitude, I, **Dr RK Bharti**, wholeheartedly thank my reverend mother, **Smt. Bangla Bai,** esteemed father, **Shri Jagdish Bharti**, beloved wife, **Dr Pratima Koshewara**, cherished son, Navyn, adorable daughter, Xiona, and all my cherished family members for their boundless blessings, unwavering inspiration, and steadfast encouragement that have illuminated every milestone of my life and distinguished career.

I, **Dr Vikas Sood**, express my profound gratitude to my parents, my wife **Mrs Babita Sood**, daughter **Ms Vasvi Sood,** son **Suryansh Sood** and all my family members for their patience, unfailing support and cooperation throughout this work period.

We all express our profound gratitude from the core of our heart to our families for their constant support and encouragement as they were the source of inspiration for us to accomplish this project.

We would like to thank **Mr Satish Kumar Jain** (Chairman) and **Mr Varun Jain** (Managing Director), M/s CBS Publishers and Distributors Pvt Ltd for providing us the platform in bringing out the book.

We sincerely thank the entire CBS team for bringing out the book with utmost care and attractive presentation. We would like to thank Ms Nitasha Arora (Assistant General Manager – Publishing) and Dr Anju Dhir (Sr. Product Manager cum Commissioning Editor) for their publishing support. We would also like to extend our thanks to Ms Surbhi Gupta (Sr. Editor cum Team Lead, Mr Ashutosh Pathak (Assistant Production Manager cum TL) and all the production team members for devoting laborious hours in editing, designing and typesetting the book.

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The name of the reviewers are arranged in alphabetical order.

Special Features of the Book

LEARNING OBJECTIVES

After studying the chapter, readers will be able to:

- Describe the principles of pharmacodynamics, pharmacokinetics, classification, and the principles of drug administration.
- Understand the effects of microsomal enzymes.
- Classify the types of drug formulations.

Learning Objectives given in the beginning of each chapter enable the student to know what he/she will learn after reading.

Every chapter begins with a **Chapter Outline** to provide a glimpse of the content discussed.

CHAPTER OUTLINE

- Introduction
- Definitions
- Sources of Drugs
- Systems of Measurement
- Terminology Used

3 CASE SCENARIO

A 40-year-old mild obese man had routine health check-up and was found to have low HDL, high LDL and TG for which the treating physician prescribed rosuvastatin 10 mg OD and nicotinic acid 100 mg TDS with regular exercise. After 2 weeks of therapy,

3 Case Scenario Explanation

This is the case of mixed dyslipidemia where the level of HDL is low and LDL, TG levels were high. In mixed dyslipidemia,

Each and every topic has been introduced with **Clinical Case Scenario** along with its explanation from theoretical and clinical integration point of view.

Numerous **Figures** are used to make learning easy for students.

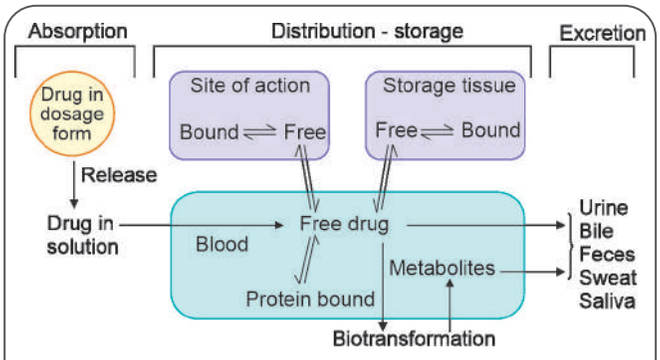


Fig. 1.2: Diagrammatic presentation of pharmacokinetics of a drug

Must Know

Additive Drug Combinations

- Aspirin + paracetamol as analgesic/antipyretic
- Amlodipine + atenolol as antihypertensive
- Glibenclamide + metformin as hypoglycemic

Important information that needs attention has been highlighted in **Must Know** boxes.

Various **Tables** are used to help students grasp the concepts quickly.

Table 8.16: Dose and duration of tinidazole in various indications

Indications	Dose and duration
Intestinal amoebiasis	2 g OD for 3 days (children 30–50 mg/kg/day) or 0.6 g BD for 5–10 days
Amoebic liver abscess	2 g daily for 3–6 days
Trichomoniasis and giardiasis	2 g single dose or 0.6 g OD for 7 days

Drug-to-drug interactions have been given separately to help the nurses during their practice.

Drug Interactions

- The levels of digoxin and warfarin are increased by amiodarone by reducing their renal clearance.
- Amiodarone can produce additive A-V block, if given along with calcium channel blockers or β-blockers.

Nursing Implications enlist the various measures required by nurses while administering the drugs of every class.

NURSING IMPLICATIONS

Nursing Implications for Histamines

Administer the drug apart from any other oral medications approximately 1 hour before or 2-hour after to ensure adequate absorption of the other medications.

- Administer drug before meals to ensure the therapeutic effectiveness of the drug.
- Monitor the patient continually if giving IV doses to allow early detection of potentially serious adverse effects, including cardiac arrhythmias.

STUDENT ASSIGNMENT

Detailed **Student Assignment** in the form of exercises in each and every chapter will facilitate structured learning and revision of the material provided in the respective chapters.

LONG ANSWER QUESTIONS

1. What is a drug? Describe the various sources of drugs.
2. Explain the various routes of drug administration.

SHORT ANSWER QUESTIONS

1. Write short notes on:
   a. Pharmacokinetics
   b. Pharmacodynamics
   c. First pass metabolism
2. What do you understand by the kinetics of elimination?

MULTIPLE CHOICE QUESTIONS

1. **Alkalinization of urine is required for decreasing the poisoning due to:**
   a. Barbiturates
   b. Amphetamine
   c. Alcohol
   d. Morphine

Syllabus

Pharmacology–I

Placement: III Semester **Theory:** 1 Credit (20 Hours)

Unit	Time (Hrs)	Learning Outcomes	Content	Teaching/Learning Activities	Assessment Methods
I	3 (T)	Describe pharmacodynamics, pharmacokinetics, classification, principles of administration of drugs	**Introduction to Pharmacology** • Definitions and branches • Nature and sources of drugs • Dosage forms and routes of drug administration • Terminology used • Classification, abbreviations, prescription, drug calculation, weights and measures • *Pharmacodynamics:* Actions, drug antagonism, synergism, tolerance, receptors, therapeutic, adverse, toxic effects, pharmacovigilance • *Pharmacokinetics:* Absorption, bioavailability, distribution, metabolism, interaction, excretion • Review: Principles of drug administration and treatment individualization ▪ Factors affecting dose, route etc. • Indian pharmacopoeia: Legal issues, drug laws, schedule drugs • Rational use of drugs • Principles of therapeutics	• Lecture cum discussion • Guided reading and written assignment on schedule K drugs	• Short answer • Objective type • Assessment of assignments
II	1 (T)	Describe antiseptics, and disinfectant and nurse's responsibilities	**Pharmacology of Commonly Used Antiseptics and Disinfectants** • Antiseptics and disinfectants • Composition, action, dosage, route, indications, contraindications, drug interactions, side effects, adverse effects, toxicity and role of nurse	• Lecture cum discussion • Drug study/ presentation	• Short answer • Objective type
III	2 (T)	Describe drugs acting on gastrointestinal system and nurse's responsibilities	**Drugs Acting on GI System** • Pharmacology of commonly used drugs ▪ Emetics and antiemetics ▪ Laxatives and purgatives ▪ Antacids and antipeptic ulcer drugs ▪ Antidiarrheals—fluid and electrolyte therapy, furazolidone, dicyclomine • Composition, action, dosage, route, indications, contraindications, drug interactions, side effects, adverse effects, toxicity and role of nurse	• Lecture cum discussion • Drug study/ presentation	• Short answer • Objective type
IV	2 (T)	Describe drugs acting on respiratory system and nurse's responsibilities	**Drugs Acting on Respiratory System** • Pharmacology of commonly used ▪ Antiasthmatics—Bronchodilators (Salbutamol inhalers)	• Lecture cum discussion • Drug study/ presentation	• Short answer • Objective type

Contd...

Unit	Time (Hrs)	Learning Outcomes	Content	Teaching/Learning Activities	Assessment Methods
			▪ Decongestants ▪ Expectorants, antitussives and mucolytics ▪ Bronchoconstrictors and antihistamines • Composition, action, dosage, route, indications, contraindications, drug interactions, side effects, adverse effects toxicity and role of nurse		
V	4 (T)	Describe drugs used on cardiovascular system and nurse's responsibilities	**Drugs Used in Treatment of Cardiovascular System and Blood Disorders** • Hematinics, and treatment of anemia and antiadrenergics • Cholinergic and anticholinergic • Adrenergic drugs for CHF and vasodilators • Antianginals • Antiarrhythmics • Antihypertensives • Coagulants and anticoagulants • Antiplatelets and thrombolytics • Hypolipidemics • Plasma expanders and treatment of shock • Drugs used to treat blood disorders • Composition, action, dosage, route, indications, contraindications, drug interactions, side effects, adverse effects, toxicity and role of nurse	• Lecture cum discussion • Drug study/ presentation	• Short answer • Objective type
VI	2 (T)	Describe the drugs used in treatment of endocrine system disorders	**Drugs Used in Treatment of Endocrine System Disorders** • Insulin and oral hypoglycemics • Thyroid and antithyroid drugs • Steroids ▪ Corticosteroids ▪ Anabolic steroids • Calcitonin, parathormone, vitamin D_3, calcium metabolism ▪ Calcium salts	• Lecture cum discussion • Drug study/ presentation	• Short answer • Objective type
VII	1 (T)	Describe drugs used in skin diseases and nurse's responsibilities	**Drugs Used in Treatment of Integumentary System** • Antihistaminics and antipruritics • Topical applications for skin—benzylbenzoate, gamma BHC, clotrimazole, miconazole, silver sulphadiazine (burns) • Composition, action, dosage, route, indications, contraindications, drug interactions, side effects, adverse effects toxicity and role of nurse	• Lecture cum discussion • Drug study/ presentation	• Short answer • Objective type

Contd...

Unit	Time (Hrs)	Learning Outcomes	Content	Teaching/Learning Activities	Assessment Methods
VIII	5 (T)	Explain drug therapy/ chemotherapy of specific infections and infestations and nurse's responsibilities	**Drugs Used in Treatment of Communicable Diseases (Common Infections, Infestations)** • General principles for use of antimicrobials • Pharmacology of commonly used drugs: ▪ Penicillin, cephalosporins aminoglycosides, macrolide and broad spectrum antibiotics, sulfonamides, quinolones, misc. antimicrobials • Anaerobic infections • Antitubercular drugs • Antileprosy drugs • Antimalarials • Antiretroviral drugs • Antiviral agents • Antihelminthics, antiscabies agents • Antifungal agents • Composition, action, dosage, route, indications, contraindications, drug interactions, side effects, adverse effects, toxicity and role of nurse	• Lecture cum discussion • Drug study/ presentation	• Short answer • Objective type

Pharmacology–II
Including Fundamentals of Prescribing Module

Placement: IV Semester

Theory: 3 Credit (60 Hours)

Unit	Time (Hrs)	Learning Outcomes	Content	Teaching/Learning Activities	Assessment Methods
I	4 (T)	Describe drugs used in disorders of ear, nose, throat and eye and nurse's responsibilities	**Drugs used in Disorders of Ear, Nose, Throat and Eye** • Antihistamines • Topical applications for eye (chloramphenicol, gentamycin eye drops), ear (soda glycerin, boric spirit ear drops), nose and buccal cavity-chlorhexidine mouthwash • Composition, action, dosage, route, indications, contraindications, drug interactions, side effects, adverse effects, toxicity and role of nurse	• Lecture cum discussion • Drug study/ presentation	• Short answer • Objective type
II	4 (T)	Describe drugs acting on urinary system and nurse's responsibilities	**Drugs Used on Urinary System** • Pharmacology of commonly used drugs ▪ Renin angiotensin system ▪ Diuretics and antidiuretics ▪ Drugs toxic to kidney ▪ Urinary antiseptics ▪ Treatment of UTI—acidifiers and alkalinizers • Composition, action, dosage, route, indications, contraindications, drug interactions, side effects, adverse effects toxicity and role of nurse	• Lecture cum discussion • Drug study/ presentation	• Short answer • Objective type

Contd...

Unit	Time (Hrs)	Learning Outcomes	Content	Teaching/Learning Activities	Assessment Methods
III	10 (T)	Describe drugs used on nervous system and nurse's responsibilities	**Drugs Acting on Nervous System** • Basis and applied pharmacology of commonly used drugs • Analgesics and anesthetics ▪ Analgesics: Nonsteroidal anti-inflammatory (NSAID) drugs ▪ Antipyretics ▪ Opioids and other central analgesics ◆ General (techniques of GA, pre-anesthetic medication) and local anesthetics ◆ Gases: Oxygen, nitrous, oxide, carbondioxide and others • Hypnotics and sedatives • Skeletal muscle relaxants • Antipsychotics ▪ Mood stabilizers • Antidepressants • Antianxiety drugs • Anticonvulsants • Drugs for neurodegenerative disorders and miscellaneous drugs • Stimulants, ethyl alcohol and treatment of methyl alcohol poisoning • Composition, action, dosage, route, indications, contraindications, drug interactions, side effects, adverse effects toxicity and role of nurse	• Lecture cum discussion • Drug study/ presentation	• Short answer • Objective type
IV	5 (T)	Describe drugs used for hormonal disorder and supplementation, contraception and medical termination of pregnancy and nurse's responsibilities	**Drugs Used for Hormonal, Disorders and Supplementation, Contraception and Medical Termination of Pregnancy** • Estrogens and progesterones ▪ Oral contraceptives and hormone replacement therapy • Vaginal contraceptives • Drugs for infertility and medical termination of pregnancy ▪ Uterine stimulants and relaxants • Composition, actions, dosage, route, indications, contraindications, drug interactions, side effects, adverse effects, toxicity and role of nurse	• Lecture cum discussion • Drug study/ presentation	• Short answer • Objective type
V	3 (T)	Develop understanding about important drugs used for women before, during and after labor	**Drugs Used for Pregnant Women during Antenatal, Labor and Postnatal Period** • Tetanus prophylaxis • Iron and vitamin K1 supplementation • Oxytocin, misoprostol • Ergometrine • Methyl prostaglandin F2-alpha • Magnesium sulfate • Calcium gluconate	• Lecture cum discussion • Drug study/ presentation	• Short answer • Objective type

Contd...

Unit	Time (Hrs)	Learning Outcomes	Content	Teaching/Learning Activities	Assessment Methods
VI	10 (T)	Describe drugs used in deaddiction, emergency, poisoning, vitamins and minerals supplementation, drugs used for immunization and immune-suppression and nurse's responsibilities	**Miscellaneous** • Drugs used for deaddiction • Drugs used in CPR and emergency—adrenaline, chlorpheniramine, hydrocortisone, dexamethasone • IV fluids and electrolytes replacement • Common poisons, drugs used for treatment of poisoning ▪ Activated charcoal ▪ Ipecac ▪ Antidotes ▪ Anti-snake venom (ASV) • Vitamins and minerals supplementation • Vaccines and sera (Universal immunization program schedules) • Anticancer drugs: Chemotherapeutic drugs commonly used • Immunosuppressants and immunostimulants	• Lecture cum discussion • Drug study/ presentation	• Short answer • Objective type
VII	4 (T)	Demonstrate awareness of common drugs used in alternative system of medicine	**Introduction to Drugs Used in Alternative Systems of Medicine** • Ayurveda, Homeopathy, Unani and Siddha, etc. • Drugs used for common ailments	• Lecture cum discussion • Observational visit	• Short answer • Objective type
VIII	20 (T)	Demonstrate understanding about fundamental principles of prescribing	**Fundamental Principles of Prescribing** • Prescriptive role of nurse practitioners: Introduction • Legal and ethical issues related to prescribing • Principles of prescribing • Steps of prescribing • Prescribing competencies	Completion of module on fundamental principles of prescribing	• Short answer • Assignment evaluation

Contents

10

Drugs Acting on Urinary System

LEARNING OBJECTIVES

After studying the chapter, readers will be able to:

- Describe process of urine formation.
- Differentiate diuretics and antidiuretics.
- Explain the role of the osmoreceptor in fluid balance.
- Discuss the function and regulation of the antidiuretic hormone.
- Understand the use of urinary acidifiers and alkalinizers.
- Outline the management of UTI and STDs.

CHAPTER OUTLINE

- Diuretics and Antidiuretic Drugs
- Urinary Antiseptics
- Cholinergic and Anticholinergic Drugs Used in Urinary System
- Acidifiers and Alkalinizers
- Sexually Transmitted Diseases

Note: For renin angiotensin system, refer to the Chapter 5.

DIURETICS AND ANTIDIURETIC DRUGS

1 CASE SCENARIO

A 45-year-old male had hypertension which was not managed by single antihypertensive drug. The doctor added tablet hydrochlorothiazide with ACE inhibitor. Now he is presented in casualty with complaint of cramping and severe muscle weakness. Which drug is responsible for the emergence of such condition?

Renal Physiology

Kidney is the main excretory organ of our body. Normally, we have a pair of kidneys. *Nephron* is the smallest functional unit of kidney. Approximately 1–1.5 million nephrons constitute one kidney.

The main functions of kidneys are as follows:

- **Excretory function:** Excretion of nitrogenous wastes, such as urea, uric acid, creatinine, etc.
- **Regulatory function:** It regulates and maintains the balance of fluid and electrolyte mainly. It also maintains the blood pressure and acid-base balance.
- **Hormonal function:** Production of erythropoietin and renin, activation of vitamin D.
- The kidneys receive approximately 20–25% of cardiac output, out of which 10% is filtered in the glomeruli and is known as *glomerular filtrate*.
- Normally both kidneys filter nearly 125 mL fluid per minute. This is called glomerular filtration rate.
- The kidneys filter approximately 180 L of fluid/day, out of which 99% is reabsorbed and 1% (i.e., 1.8 L) is excreted out in the form of urine.

Urine formation involves mainly three processes:

i. **Glomerular filtration:** It is a process of filtration of plasma through the glomerulus into tubules of nephron.
ii. **Selective tubular reabsorption:** It is a process of selective water and solutes reabsorption from the tubular fluid.
iii. **Tubular secretion:** It is a process where solutes are secreted into the tubular fluid. Mostly, those solutes are secreted which cannot be filtered through glomerulus.

The net volume of urine formation is affected by above three processes.

The diuretic and antidiuretic drugs affect the urine formation by acting at the different parts of nephron. The drugs mainly affect selective reabsorption process.

The different sites of drug action are as follows:

Site I: Proximal convoluted tubule

Site II: Thick ascending limb of loop of Henle

Site III: Cortical diluting segment of loop of Henle

Site IV: Distal convoluted tubule and collecting duct.

Diuretics

The drugs, which increase the excretion of urine by their action on the kidneys (specifically nephrons), are called *diuretics*. This is achieved mainly by increasing the loss of sodium and water.

Classification of Diuretics

The classification of diuretics is based upon the site of nephron on which they act (Fig. 10.1). The different diuretics are as follows:

- **Drugs acting on site I or proximal convoluted tubule or Carbonic anhydrase inhibitors:** Acetazolamide.
- **Drugs acting on site II or thick ascending limb of loop of Henle or loop diuretics:** Furosemide, bumetanide, torasemide, ethacrynic acid, indacrinone.
- **Drugs acting on site III:** Cortical diluting segment of loop of Henle or early DCT or thiazides and thiazide like diuretics:
  - **Thiazide diuretics:** Hydrochlorothiazide, chlorothiazide, clopamide, bendroflumethiazide, benzthiazide.
  - **Thiazide-like diuretics:** Chlorthalidone, indapamide, xipamide, metolazone, quinethazone.
- **Drugs acting on Site IV:** Late DCT and collecting duct (CD) or potassium sparing diuretics:
  - Aldosterone receptor antagonists: Spironolactone and eplerenone.
  - Na^+ channel inhibitors (at collecting duct): Triamterene and amiloride.
- Drugs acting on entire nephron or osmotic diuretics: mannitol, isosorbide, glycerol, etc.

Classification of diuretics according to their efficacy is given in Table 10.1.

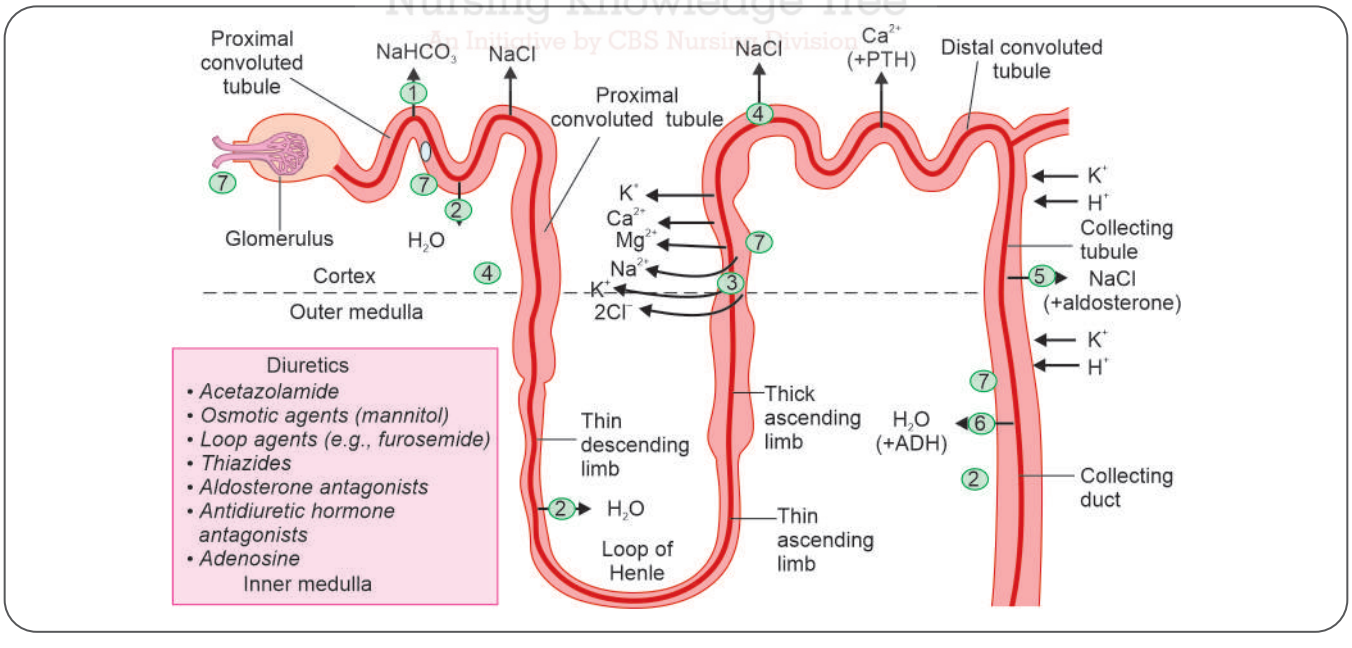


Fig. 10.1: Action of diuretics on tubular transport system

Table 10.1: Classification according to efficacy of diuretics

High-efficacy diuretics	Medium efficacy diuretics	Weak or adjunctive diuretics
Na^+ $K^{+2}Cl^-$ cotransport Inhibitors	**Na^+Cl^- symport Inhibitors**	• Inhibitors of carbonic anhydrase enzyme: Acetazolamide • **Potassium sparing diuretics:** ▪ Aldosterone receptor antagonist ▪ Spironolactone ▪ Eplerenone • **Na^+ channel inhibitors (at collecting duct):** ▪ Triamterene ▪ Amiloride • **Osmotic diuretics:** ▪ Mannitol ▪ Glycerol ▪ Isosorbide
• Furosemide • Torsemide • Bumetanide • Indacrinone • Ethacrynic acid	**Thiazide's diuretics:** • Hydrochlorothiazide • Chlorothiazide • Benzthiazide, • Hydroflumethiazide, Bendroflumethiazide **Thiazide-like diuretics:** • Chlorthalidone • Indapamide • Xipamide • Metolazone • Quinethazone	

Drugs Acting on Site-I or Proximal Convoluted Tubule

[Weak or adjunctive diuretics or (Carbonic anhydrase inhibitors)]

Carbonic Anhydrase (CAse) Inhibitors

(Acetazolamide)

Carbonic anhydrase inhibitors are weak diuretics and have some other pharmacological actions also.

The various sites where carbonic anhydrase enzyme is present are:

- Kidney: Renal tubular cells of proximal tubules
- GIT: Gastric mucosa exocrine pancreas
- Eye: Ciliary body of eye
- Brain
- Blood: RBCs

In these tissues, a gross excess of case is present and >99% inhibition is required to produce clinical effects.

Methazolamide and Dichlorphenamide are some other systemic case inhibitors, whereas, Dorzolamide and Brinzolamide are topical case inhibitors used in glaucoma.

Mechanism of Action

- Acetazolamide is a noncompetitive reversible inhibitor of both membrane-bound and cytoplasmic forms of carbonic anhydrase in PCT.
- Inhibition of carbonic anhydrase enzyme causes increased excretion of bicarbonates with Na^+, K^+ and water.
- The net result is excretion of alkaline urine due to retention of HCO^{3-} in the tubular lumen.

Extrarenal Effects of Acetazolamide

- It decreases intraocular pressure by reducing the formation of aqueous humor.
- It decreases the pH and raises CO_2 in brain; that may lead to sedation and seizures.
- It may cause CO_2 transport alteration in lungs.

Pharmacokinetics

It is well absorbed orally and excreted *via* tubular secretion. The efficacy decreases on prolonged use. It has effects on choroid plexus and ciliary body also. It is given in a dose of 250 mg OD/BD.

Indications

Because of self-limiting action (refractoriness), production of acidosis and hypokalemia, acetazolamide is not used as diuretic.

Its current clinical uses are:

- **Glaucoma:** As adjuvant to other ocular hypotensive. (Dorzolamide and Brinzolamide are used topically).
- **To increase urinary pH:** Increasing urinary pH helps to treat urate calculi, cystinuria and urinary tract infections
- **Mild metabolic alkalosis:** Can be treated as they cause hyperchloremic acidosis.
- **Epilepsy:** As adjuvant in absence seizures when primary drugs are not fully effective.
- **Acute mountain sickness syndrome:** It has both prophylactic and therapeutic value.

Adverse Effects

- The common side effects are: Hyperchloremic acidosis, drowsiness, paresthesias, fatigue, hypokalemia and abdominal discomfort.
- Refractoriness is also a major disadvantage.
- Acetazolamide is contraindicated in hepatic cirrhosis patients.

Drugs Acting on Site-II or Thick Ascending Limb of Loop of Henle or Loop Diuretics/High-Efficacy Diuretics/High-Ceiling Diuretics

(Inhibitors of Na^+- K^+-$2Cl^-$ cotransport)

- All the drugs of this class primarily act on the site II or the thick ascending limb of Henle's loop. Therefore, these are called *loop diuretics.*
- The diuretic response increases as we go on increasing the dose, hence called *high-ceiling diuretics.*
- The efficacy of these drugs has been rated as highest amongst all diuretic agents, hence also called *high-efficacy diuretics.*
- These drugs are capable of producing up to 10 L of urine in a day.
- These agents have very fast and short duration of action.

Mechanism of Action

- When given by oral/IM or IV route, these drugs on reaching the circulation get bound to plasma proteins and cannot pass through glomerulus.
- These drugs reach their site of action (thick ascending limb of loop of Henle) by the process of proximal tubular secretion and act from the luminal side.
- These drugs inhibit Na^+ - K^+- $2Cl^-$ cotransport at site II and inhibit the reabsorption of NaCl out of the tubule into the interstitial space. Thus, the increased Na^+ and Cl^- reach the distal tubule and promote the loss of H^+ and K^+ along with increased loss of water causing profuse diuresis.
- The excretion calcium and magnesium also increase.
- Intravenous furosemide transiently decreases preload by increasing systemic venous capacitance or peripheral pooling. This action is prostaglandin mediated and is responsible for the quick relief in left ventricular failure and pulmonary edema.

Furosemide or Frusemide

- Furosemide is the most efficacious of all diuretics.
- It is well absorbed orally with 60% of bioavailability.
- It is highly plasma protein bound and eliminated partly through glomerular filtration and partly through tubular secretion. Some part is directly excreted in intestines through bile also.
- It has very rapid onset of action, i.e., within 2–5 minutes after IV administration, 10–20 minutes after IM route and 20–40 minutes after oral administration.
- The t½ is 1–2 hours with maximum duration of action 3–6 hours.
- It is given in a dose of 20–80 mg by oral route once daily in the morning.
- In pulmonary edema, it is given in a dose of 40–80 mg IV.

Bumetanide

- It is 40 times more potent than furosemide with other pharmacological properties similar to furosemide.
- It is also well absorbed orally with 80–100% of bioavailability.
- The plasma t½ is 60 minutes and may prolong in patients with kidney or liver impairment.
- It is preferred in furosemide non-responders or furosemide allergic patients.
- Bumetanide is given in a dose of 1–5 mg oral route once daily in the morning and 1–4 mg by IM or IV route.

Torasemide (Torsemide)

- It is three times more potent and longer acting than furosemide.
- It is rapidly and completely absorbed by oral route with a t½ of 3.5 hours.
- The duration of action is 4–8 hours.
- It is given in a dose of 2.5–5 mg OD for hypertension and 5–20 mg/day in edema.

Ethacrynic Acid

Due to its ototoxic and hepatotoxic side effects, it has gone *out of use.*

Indacrinone

- Indacrinone is an ethacrynic acid analogue and is a uricosuric diuretic.
- It inhibits the absorption of uric acid at proximal convoluted tubule besides inhibiting Na^+-K^+-$2Cl^-$ convoluted at site II.
- It is usually preferred in the gout patients requiring diuretic therapy.

Must Know

The relative potency order of loop diuretics is:
Bumetanide > torsemide > furosemide > ethacrynic acid = Indacrinone

Indications

- **Edematous conditions:** Associated with hepatic, renal or cardiac origin. These drugs are very effective in relieving the symptoms of congestive cardiac failure, cirrhosis of liver and nephrotic syndrome immediately. Thiazides may be given later on for maintenance purpose.
- **Acute pulmonary edema:** Intravenous administration of furosemide or its congeners produces prompt relief.
- **Hypertension:** High-ceiling diuretics are indicated in hypertension only in the presence of renal insufficiency, Congestive heart failure, or in resistant cases and in hypertensive emergencies; otherwise, thiazides are preferred.
- **In massive blood transfusions:** Diuretics are given during massive blood transfusions to prevent renal overload.
- **Acute renal failure:** In renal failure cases, these drugs can convert oliguric phase of renal failure to nonoliguric phase.
- **Cerebral edema:** Intracranial pressure can be lowered by these drugs but osmotic diuretics are preferred.
- **Acute hypercalcemia:** The calcium excretion and urine flow are increased.

Adverse Effects

- Electrolyte disturbances such as hypokalemia, hyponatremia, hypocalcemia, hypomagnesemia. So, electrolyte monitoring should be done regularly.
- Metabolic disturbances such as hyperglycemia, hyperuricemia, hyperlipidemia.
- General disturbances such as nausea, vomiting, diarrhea, headache, giddiness, myalgia, etc.
- Reversible ototoxicity.
- Hypersensitivity reactions.

Drugs Acting on Site-III: Cortical Diluting Segment of Loop of Henle or Early DCT or Medium Efficacy Diuretics/Thiazides and Thiazide Like Diuretics

(Na^+Cl^- symport inhibitors)

- **Thiazide diuretics:** Hydrochlorothiazide, chlorthiazide, clopamide, bendroflumethiazide, benzthiazide.
- **Thiazide-like diuretics:** Chlorthalidone, indapamide, xipamide, metolazone, quinethazone.
- All the drugs of this class primarily act on the site III or cortical diluting segment of loop of Henle or early distal convoluted tubule.
- These are the less powerful than loop diuretics but, more powerful than other diuretic groups, hence also called *medium efficacy diuretics.*
- They have a longer duration of action as compared to loop diuretics.

Mechanism of Action

- When given by oral route, these drugs on reaching the circulation get bound to plasma proteins and cannot pass through glomerulus.
- These drugs also reach their site of action (early distal convoluted tubule) by the process of proximal tubular secretion and act from the luminal side.
- These drugs inhibit Na^+Cl^- symporter at site III and inhibit the reabsorption of NaCl out of the tubule into the interstitial space. This increases the loss of NaCl with water in the form of urine.
- Some of the thiazides and related drugs have additionally weak carbonic anhydrase inhibitory action in proximal convoluted tubule.
- They inhibit urinary excretion of calcium and uric acid.
- There are no injectable preparations of these drugs.

Hydrochlorothiazide

- The t½ of hydrochlorothiazide is 3–6 hours.
- In hypertension, it is given in a dose of 12.5–50 mg/day.
- In edema patients, it is given in a dose of 25–100 mg/day.

Chlorthalidone

- It is a nonthiazide, but thiazide-like diuretic and behaves pharmacologically, like hydrochlorothiazide.
- The plasma t½ is 40–50 hours.
- In hypertension, it is given orally in a dose of 12.5–50 mg once daily, preferably in the morning.

Metolazone

- Metolazone has a special property that it works even in severe renal failure patients with a GFR of ≤15 mL/min.
- It has a synergistic effect when given with furosemide.
- In edema, it is given orally in a dose of 5–10 mg/day.
- In hypertension, it is given orally in a dose of 2.5–5 mg/day.

Xipamide

- Its pharmacological action is similar to low doses of furosemide.
- Its duration of action is approximately 12 hours and is given in a dose of 20–40 mg/day.
- The dose given in hypertension is 10–20 mg/day and in edema is 40–80 mg/day.
- It may cause severe hypokalemia sometimes.

Indapamide

- It is a lipid soluble thiazide and has very little diuretic action, but retains some antihypertensive action for which it is still used in some cases.
- It is given in a dose of 2.5–5 mg OD and has duration of action 12–34 hours.

Must Know

The relative potency of Thiazides and thiazide-like diuretics is:
Indapamide > Bendroflumethiazide > Metolazone > hydrochlorothiazide = Chlorthalidone > chlorothiazide
The duration of action rank order of Thiazides and thiazide-like diuretics is:
Chlorthalidone > Indapamide = Metolazone > Bendroflumethiazide > Hydrochlorothiazide > chlorothiazide

Indications

- **Hypertension:** Thiazides and related diuretics, especially chlorthalidone and hydrochlorothiazide are one of the first-line drugs in hypertension in elderly. The fall in BP develops gradually over 2–4 weeks. The maximum antihypertensive efficacy is reached at a dose of 25 mg/day.
- **Edema:** Thiazides may be used for mild to moderate cases. To start with, more efficacious diuretics are preferred to mobilize the edema fluid and thiazides are used for maintenance therapy. They act best in cardiac edema and are less effective in hepatic or renal edema.
- **Diabetes insipidus:** Thiazides reduce the urine volume in patients of diabetes insipidus. This is a paradoxical effect. These are the only drugs effective in nephrogenic diabetes insipidus. However, these drugs reduce the volume of urine in patients of central diabetes also.
- **Hypercalciuria:** Thiazides inhibit urinary Ca^+ excretion and are useful in idiopathic hypercalciuria. Therefore, these drugs are beneficial for patients suffering from recurrent calcium oxalate stones.

Adverse Effects

- Electrolyte disturbances such as hypokalemia, hyponatremia, hypomagnesemia occur. In contrast to loop diuretics, these disturbances cause hypercalcemia. So, electrolyte monitoring should be done regularly.
- Metabolic disturbances, such as hyperglycemia, hyperuricemia, hyperlipidemia is similar to loop diuretics.
- Hypersensitivity reactions, such as rashes and photosensitivity reactions occur in sulfonamide sensitive patients.
- General disturbances such as nausea, vomiting, diarrhea, headache, giddiness, myalgia, etc.
- Reversible erectile dysfunction is seen as an idiosyncratic reaction in some patients.
- Loop diuretics are the drugs, which cause maximum sodium loss.
- Ethacrynic acid causes maximum loss of chloride ions in urine.
- Acetazolamide causes maximum loss of potassium and uric acid in urine and this is only drug that causes chloride reabsorption.

Differences between high and moderate efficacy diuretics are given in Table 10.2.

Table 10.2: Differences between high and moderate efficacy diuretics

Properties	High-efficacy diuretics	Moderate efficacy diuretics
Mode of action	Na^+-K-$2Cl^-$ cotransport inhibitors	Na^+-Cl^- symport inhibitors
Site of action	Thick ascending loop of Henle	Distal convoluted tubule
Role in calcium metabolism	Increase Ca^+ excretion	Increase Ca^+ reabsorption
Ototoxicity	+++	+
Role in CHF	Commonly used	Not used; but indapamide may be useful
Role in renal failure	Most preferred diuretics	Not used; but metolazone many be used

Contd...

Properties	High-efficacy diuretics	Moderate efficacy diuretics
Role in hypertension	Not preferred	Most preferred diuretics; it decreases the total peripheral resistance resulting decrease in BP
Hyperuricemia	Most preferred	Not preferred
Both groups of drugs may cause hypomagnesemia, hyponatremia, hypokalemia, hyperuricemia, hyperlipidemia and hyperglycemia.		

Drugs Acting on Site-IV: Late DCT and Collecting Duct (CD) or Potassium Sparing Diuretics

These drugs retain K^+ ions while maintain the diuretic effects. These are preferably given along with loop diuretics to prevent the potassium loss.

- **Aldosterone receptor antagonists:** Spironolactone and eplerenone.
  Spironolactone and *eplerenone* produce diuretic effects by antagonizing mineralocorticoid receptors.
- **Na^+ channel inhibitors (at collecting duct):** Triamterene and amiloride.
  Amiloride and *Triamterene* produce diuretic effects by antagonizing luminal sodium channel at distal part and collecting tubules.

Aldosterone Receptor Antagonists
(Spironolactone and Eplerenone)

Spironolactone

- It is a competitive inhibitor of mineralocorticoid receptors.
- Spironolactone competitively antagonizes the aldosterone. Hence, prevents the sodium and water reabsorption and causes diuresis.
- As sodium reabsorption is inhibited, the concomitant potassium secretion into the tubules does not take place. Hence, the potassium sparing effect is obtained.

Pharmacokinetics

- It is partially absorbed with only 65% of bioavailability *(the microfine form of tablet has 75% bioavailability)*.
- It is metabolized in liver converted to active metabolite *Canrenone*.
- It also undergoes enterohepatic circulation.
- The t½ of spironolactone is 1–2 hours, while that of canrenone is ~18 hours.
- The t½ may increase in case of cirrhosis.
- It is given in a dose of 25–50 mg BD–QID and the maximum dose ≤200 mg/day.

Indications

- It is used in combination with high-efficacy diuretics to compensate the K^+ loss in urine.
- Edema due to cirrhosis of liver and nephrotic syndrome: *Aldosterone levels are high in these conditions.*
- Congestive heart failure and hypertension: As an adjuvant to other diuretics to prevent hypokalemia.
- Conn's syndrome.
- Ectopic aldosterone production (secondary aldosteronism).

Adverse Effects

- The common side effects are hyperkalemia, epigastric distress, loose motions, and mental confusion.
- It may also cause gynecomastia and erectile dysfunction in males, while menstrual irregularities in females.

Eplerenone

- It is a newer agent having more specific antagonistic property toward the mineralocorticoid receptors. Therefore, the incidence of hormonal adverse effects is lesser than spironolactone.
- The oral absorption is good, metabolism occurs in liver and excretion through urine and feces.
- The plasma t½ is 4–6 hours.
- It is given orally in a dose of 25–50 mg BD.

Indications

- Acute myocardial infarction with left ventricular systolic dysfunction.
- Congestive heart failure
- Hypertension

Na^+ Channel Inhibitors (Act at Collecting Duct)

(Triamterene and Amiloride)

- These drugs act by inhibiting the renal epithelial Na^+ channel and increase Na^+ excretion with retention of K^+ ions.
- They also reduce the excretion of Ca^{2+} and Mg^{2+} ions without changing renal hemodynamics.

Triamterene

- Oral absorption of triamterene is partial.
- It is metabolized in liver and excretion occurs through urine with t½ of 4 hours.
- It is given orally in a dose of 50–100 mg OD.
- The common side effects are nausea, muscle cramps and dizziness.

Amiloride

- It is 10 times more potent than triamterene.
- The oral absorption is very poor.
- The metabolism occurs in liver and excretion occur through urine.
- The plasma t½ is 20 hours. It is given orally in a dose of dose 5–10 mg OD/BD.
- The common side effects are hyperuricemia, headache, nausea and diarrhea.

Indications

These drugs are indicated in:

- In combination with thiazide these drugs are used to treat refractory edema.
- In hypertension, to prevent hypokalemia induced by loop diuretics.
- Lithium induces diabetes insipidus (it blocks entry of lithium by sodium channels in the collecting duct).
- Some cases of cystic fibrosis.

Drugs Acting on Entire Nephron or Osmotic Diuretics

(Mannitol, Isosorbide and Glycerol)

- These drugs mainly act in the PCT and the descending limb of loop of Henle.
- The effect of antidiuretic hormone in the collecting duct is also decreased by these agents.
- These agents also inhibit the normal water reabsorption by their osmotic effects and lead to increased urine excretion.
- The Na^+ and water reabsorption is inhibited because these drugs decrease the contact time between tubular epithelium, causing natriuresis and excessive water loss.

Mannitol

Mannitol is pharmacologically inert substance (neither absorbed nor metabolized) and administered in high dose to produce osmotic effects on tubules and/or plasma fluids. The route of administration is intravenous only (10–20% strength). The plasma t½ is 0.5–1.5 hours.

Indications

For decreasing intracranial tension (ICT) and intraocular tension (IOT): 1–2 g/kg; it takes 60–90 minutes to reduce ICT/IOT. It decreases the cerebral and ocular edema.

Table 10.3 gives the mechanism of action for renal and extra-renal diuretics.

Adverse Effects

- The most common side effect is headache; while other side effects are nausea vomiting, dehydration, hyperkalemia, hyponatremia and pulmonary edema.
- It is contraindicated in pulmonary edema, established renal failure, acute left ventricular failure, cerebral hemorrhage and congestive heart failure.

Isosorbide and Glycerol

- These osmotic diuretics can be administered by oral route.
- These are indicated in the case of cerebral edema or acute congestive glaucoma to reduce ICT or IOT, respectively.
- These are given in a dose of 0.5–1.5 g/kg as oral solution.

Table 10.3: Mechanism of action

Renal	Extra-renal
Increased osmotic pressure of glomerular filtration ↓ Increases osmolality of tubular fluid ↓ Decrease reabsorption of water and Na^+ ↓ Diuresis	When osmolarity increase in blood ↓ Increase intravascular volume ↓ Increase renal blood flow ↓ Decrease renin production ↓ Decrease aldosterone production ↓ Diuresis

Antidiuretics

Antidiuretics are the drugs that reduce urine volume. Their primary indication is *diabetes insipidus*.

Antidiuretic drugs are divided into three groups:

i. Antidiuretic hormone [Antidiuretic hormone, argenine vasopressin (AVP)], lypressin, terlipressin, desmopressin.
ii. Thiazides and amiloride.
iii. Other drugs: Indomethacin, chlorpropamide, carbamazepine.

Antidiuretic Hormone (ADH/AVP)

- Antidiuretic hormone is synthesized in the supraoptic and paraventricular nucleus of hypothalamus and secreted by the posterior pituitary along with oxytocin.
- It is secreted under some physiological stimuli, such as rise in plasma osmolarity and contraction of extracellular fluid or falling blood pressure (BP).
- Osmoreceptors regulate the rate of their release.

Table 10.4 gives the factors affecting antidiuretic release.

Must Know

Osmoreceptors

These are sensory receptors, which are present in the hypothalamus, hepatic portal system, pulmonary veins, left atrium and ventricles. The change in osmotic pressure in our body is detected by these receptors and the fluid balance is maintained by regulating the rate of ADH release.

When the blood plasma is more diluted or concentrated, the osmoreceptors expand or contract, respectively. This leads to hyperactivation of afferent neurons and send signals to the hypothalamus, which increases or decreases the secretion of antidiuretic hormone from posterior pituitary to maintain normal blood concentration.

- The human ADH is 8-arginine-vasopressin, hence also called *AVP*.
- It has a role in long-term blood pressure control by increasing the water reabsorption from the collecting duct.

Table 10.4: Factors affecting antidiuretic hormone release

Increase ADH secretion	Decrease ADH secretion
• Histamine	• Ethanol
• Neuropeptide Y	• Gamma-aminobutyric acid
• Angiotensin II	• Atrial natriuretic peptide
• Prostaglandins	• Phenytoin
• High dose morphine	• Low dose morphine
• Acetylcholine	• Haloperidol

- It can raise blood pressure by constricting the blood vessels, hence also called *vasopressin.*

ADH exerts its effects by acting through V_1 and V_2 receptors.

V_1 receptors are located in vascular smooth muscle (including that of vasa recta in renal medulla), uterine and other visceral smooth muscles, interstitial cells in renal medulla, cortical collecting duct cells, adipose tissue, brain, platelets, liver, anterior pituitary, certain areas in brain and in pancreas, etc.

Their clinical importance lies in the constriction of blood vessels mainly.

V_2 receptors are located in the collecting duct cells, ascending limb of loop of Henle cells and the endothelium of blood vessels.

Their clinical importance lies in the antidiuretic effect by increasing the water permeability of collecting duct.

Other actions of AVP are:

- Increased gastrointestinal (GI) peristalsis (large intestine)
- Uterine contractions are increased like oxytocin
- Regulation of temperature, systemic circulation and adrenocorticotropic hormone release
- Learning of tasks

Pharmacokinetics

- AVP is inactive orally because it is degraded by trypsin; therefore, it is given parenterally by IV, SC or intranasal route in a dose of 10 U/day.
- The plasma t½ is 25 minutes.

Vasopressin Analogues

(Lypressin, Terlipressin, Desmopressin)

Lypressin (8-lysine Vasopressin)

- The potency of lypressin is lesser than AVP.
- The pharmacological actions are exerted on both V_1 and V_2 receptors.
- The duration of action is about 4–6 hours.
- It is given IM/SC in a dose of 10 IU.
- The IV infusion of 20 IU diluted in 200 mL of dextrose is given over 10–20 minutes.

Desmopressin

- Desmopressin is 10–12 times more potent than vasopressin and is a selective V_2 receptor agonist.
- It is longest acting ADH (8–12 hours) with a plasma t½ of 1–2 hours.
- It is available in intranasal, oral, subcutaneous and parenteral forms.

- It is given in different doses as follows:
  - **Orally:** 0.1–0.2 mg thrice daily.
  - **Parenterally:** 2–4 µg/day by SC/IV route in divided doses.
  - **Intranasally:** Adults: 10–40 µg/day in divided doses.
  - **Pediatric:** 5–10 µg at night (HS).

Terlipressin

- It is a synthetic prodrug of vasopressin.
- The most common indication of terlipressin is bleeding esophageal varices.
- It is given in a dose of 2 mg IV may be repeated in a dose of 1–2 mg every 4–6 hours, if required.

Indications of ADH and Vasopressin Analogs

- **Diabetes insipidus:** Highly effective in central or neurogenic diabetes insipidus, whereas ineffective in renal or nephrogenic diabetes insipidus.
- **Nocturnal enuresis:** Intranasal or oral desmopressin at bedtime controls primary nocturia by reducing urine volume.
- **Hemophilia and von Willebrand's disease:** AVP release von Willebrand factor and factor VIII, which are helpful in controlling bleeding.
- All the above actions are based on V_2 receptor activation and desmopressin is the drug of choice.
- **Bleeding esophageal varices:** Vasopressin analogues stop bleeding by constricting mesenteric blood vessels and reducing blood flow through the liver to the varices, allowing clot formation.
- This action is based upon V_1 receptor activation and Terlipressin is the drug of choice.

Adverse Effects

- **Local side effects:** Nasal congestion rhinitis and epistaxis.
- **Systemic side effects:** Headache, flushing, nausea, urticaria, abdominal cramps, backache in females (due to uterine contraction) and hyponatremia.

Vasopressin Receptor Antagonists

(Conivaptan, Tolvaptan)

Conivaptan

- **Mechanism of action is** antagonism of vasopressin V_{1a} and V_2 receptors
- **Its main effects are** to antagonize the action of vasopressin (ADH).
- **Clinically useful in managing** hyponatremia in hospitalized patients.
- **Indicated in** syndrome of inappropriate ADH secretion (SIADH) and congestive heart failure due to ADH excess.
- **Route of administration** is intravenous only.
- **Common complication** is infusion site reaction.

Tolvaptan

Tolvaptan is similar to conivaptan, but more selective for vasopressin V_2 receptors; can be given orally.

Thiazide Diuretics and Amiloride

- Thiazides reduce the urine volume in patients of diabetes insipidus. This is a paradoxical effect.
- Hydrochlorothiazide 25–50 mg TDS or equivalent dose of a longer acting agent is commonly used.
- These are the only drugs effective in nephrogenic diabetes insipidus. However, these drugs reduced the volume of urine in patients of central diabetes insipidus also.
- They are valuable in renal diabetic insipidus as AVP is ineffective.

Mechanism of Action

- Thiazides induce a state of sustained electrolyte depletion so that glomerular filtrate is more completely reabsorbed iso-osmotically in PT. Furthermore, because of reduced salt reabsorption in the cortical diluting segment, a smaller volume of less diluted urine is presented to the collecting ducts and the same is passed out.
- Secondly, thiazides reduce glomerular filtration rate (GFR) and thus the fluid load on tubules.
- High-ceiling diuretics are also effective but are less desirable because of their short and brisk action.
- In lithium-induced nephrogenic diabetes insipidus, ***Amiloride*** is the most preferred drug.

Other Drugs

(Indomethacin, Chlorpropamide, Carbamazepine)

- **Indomethacin** reduces renal prostaglandin synthesis. It is used in combination with thiazide/amiloride in nephrogenic diabetes insipidus. Other nonsteroidal anti-inflammatory (NSAIDs) are less active.
- **Chlorpropamide** acts on the pancreatic β-cell of islets, promotes insulin secretion, and produces hypoglycemic effect. It also decreases urine excretion in central DI in the presence of ADH.

- **Carbamazepine** is an anticonvulsant agent. It decreases the volume of urine in central or neurogenic diabetes insipidus. The probable mechanism of action is reduction of urine formation at pituitary level. Higher doses are needed for this effect.
- **Clofibrate:** The peroxisome proliferator–activated receptors (PPARs) regulate lipid metabolism. These drugs bind to PPARs and increase the expression and activity of lipoprotein lipase enzyme, which increases the degradation of VLDL. It also improves ADH secretion in central DI.

1 Case Scenario Explanation

This patient is experiencing the symptoms of hypokalemia. As reduction in intravascular fluid stimulates aldosterone secretion, which causes excretion in potassium and hydrogen, resulting in hypokalemic metabolic alkalosis. These side effects are commonly seen with all diuretics except potassium-sparing.

Drug Interactions

- Loop diuretics and spironolactone enhance the digitalis toxicity by causing hypokalemia.
- The levels of lithium are raised by loop diuretics. Hence, the combinations should be avoided.
- Thiazides or high-ceiling diuretics are intentionally given in combination with anti-hypertensive to obtain synergistic effects.
- The combinations of high-ceiling diuretics and aminoglycoside antibiotics should be avoided as both are ototoxic and nephrotoxic in nature.
- NSAIDs decrease the effect of high-ceiling diuretics by inhibiting prostaglandin synthesis in the kidney. Hence, the combinations should be avoided.
- Spironolactone should not be given with angiotensin converting enzyme inhibitors/angiotensin II receptor blockers as fatal hyperkalemia may occur.

NURSING IMPLICATIONS

Patients Receiving Diuretics and Antidiuretics

Assessment

Baseline Assessment

- Obtain complete medical and personal history related to the diseases prior to admission. That includes history of cardiovascular (H/o previous MI, arrhythmia, valvular diseases, PCI), cerebrovascular and neurological (H/o previous head injury, stroke, CVA), respiratory, metabolic disease, drug history, drug/food allergy, OTC/herbal drugs, pregnancy or lactation and present prescription.
- Assess for contraindications or cautions: Known allergies to these drugs to avoid hypersensitivity reactions.
- Assess patients-related laboratory investigations such as CBC with PS electrolytes, glucose, LFT and RFT, lipid profile, and coagulation profile.
- Obtain appropriated baseline of vital signs (especially BP), ECG (rate and rhythm), urinary output, cardiac output, bowel sound, height and weight.
- Assess any sign of bleeding, and patient or caregiver ability to understand instruction.

Assessment During Drug Administration

- During drug administration, nurses should monitor patient's hemodynamic status.
- Also monitor the therapeutic effect of drugs such as BP comes to prescribed normal limits and adequate urine output.
- Nurse should monitor the pulse, blood pressure, electrocardiogram (ECG), respiratory rate before, during and after the therapy.
- The treating physician should be informed immediately about any abnormal deviation (low/high) of the blood pressure.
- Never leave the patient unattended when the IV drip is going-on.

Nursing diagnosis

- Reduced cardiac output
- Fatigue
- Hypovolemia
- Poor knowledge about medicines
- Drug-related side effects, like urge incontinence, intolerance

Contd...

Assessment

- Have emergency life support equipment readily available in case of severe reaction to the drug or myocardial infarction.
- It is highly important to observe any side effect such as nausea, sexual dysfunction, fatigue, dizziness, myalgia, arthralgia, numbness/tingling sensation on extremities during drug administration and in case of severe hypotension, reflex tachycardia, bradycardia, imbalance or improper muscles coordination and reduce urinary output immediately reported to the treating physician.

Nursing diagnosis

Patient-related goals and outcomes

- The patients:
  - Will observe the therapeutic outcome of given drugs, like decreased BP to established parameters as prescribed normal limits and adequate urine output.
  - Can have negligible drug-induced side effects.
  - Can express the indications, side effects and precaution of given drugs.
  - Can self-administer drug in prescribed dose and timing.

Nursing interventions

To Ensure Drug Therapeutic Effect

- It is mandatory to observe patient frequently for any drug-induced effect. Patient's hemodynamic status should be maintained in a normal level as set by the physician.
- Asses the therapeutic effect of given drugs as reduction in BP comes to prescribed normal limits and symptomatic relieve in associated diseases.
- Continuously monitor urinary output, cardiac response, and heart rhythm of patients receiving intravenous diuretics to monitor for electrolyte disturbances leading to cardiac arrhythmia.
- Assure that route of administration is appropriate for each patient to ensure therapeutic effects and decrease adverse effects.
- Supportive measures should be provided by nursing staff, that improves the patient's compliance and better outcome.
- Follow and teach appropriate technique of routes of administration.

Minimize Side Effects

- If patient is not catheterized, administer oral/injectable diuretics early in the day so that increased urination will not interfere with sleep.
- The pulse of the patient on diuretic therapy should be palpated carefully to assess the ectopic beats and if noted should be brought into the notice of physician.
- Frequent monitoring is advocated of vital signs specially among elder patients; as these agents cause orthostatic hypotension. Nurse should be cautious while handling elderly patient with H/o CVA. Take BP on standing, sitting and lying position to detect any development in orthostatic hypotension.
- Monitor patient's electrolyte levels such as sodium, potassium, blood glucose, RFT, LFT and take ECG periodically. Hypokalemia or hyperkalemia can cause dysrhythmias.
- Frequent monitor patient weigh and inform treating physician for fluid retention; that can be done by taking the weight of the patient in the same clothes at the same time each day (weight of the patient increase by 1 kg within 24 hours). Assess dependent areas for edema and note the amount and degree of pitting to evaluate the severity of fluid retention.

Patient-centered care

- Educate patient and their relative/caregiver about how to take BP by sphygmomanometer, pulse and make sure the all equipment is well functioning and calibrated.
- Encourage patient to implement lifestyle changes, including weight loss, smoking cessation, decreased alcohol and salt in the diet, and increased exercise, to increase the effectiveness of antihypertensive therapy.
- Educate and instruct patient to start physical activities, like yoga, pranayama, walking, and avoid strenuous exercise.
- Evaluate the effectiveness of the teaching plan (patient can name drug, dosage, proper administration, adverse effects to watch for, specific measures to avoid them, and the importance of continued follow-up).
- Educate patients to rise slowly from sitting/lying to avoid dizziness or postural hypotension.
- Patient should be educated that; thiazide diuretics may cause photosensitivity. Wear sunglasses in bright light.
- Instruct patient not to take antihypertensive if BP is <90/60 mm Hg and contact treating physician.
- Instruct patient to monitor his weight on regular basis; contact treating physician if weight increases by 1 kg within 24 hours and development of edema.
- Educate and instruct the patient to take potassium-rich diet (banana, dry fruits, strawberry, apricots, etc.), if they are taking thiazides, thiazide-like, and loop diuretics.
- Instruct the patient to avoid potassium- rich product, if he/she is on potassium sparing diuretics.
- Instruct patient to take plenty of liquid but not overload it; stay hydrated and take fiber rich diet.

Contd...

Nursing interventions	Patient-centered care
• Monitor patient for any hearing problem such as vertigo or tinnitus and electrolyte imbalance; as loop diuretics are associated with ototoxicity and potassium-spearing diuretics responsible for hyponatremia. • Periodically check blood glucose level, as loop diuretics and thiazides are associated with hyperglycemia. • Monitor for adverse effects nausea, sexual dysfunction, fatigue, dizziness, myalgia, arthralgia, numbness/tingling sensation on extremities, hypotension, reflex tachycardia, bradycardia, imbalance or improper muscles coordination and reduce urinary output.	Advise and instruct patient and his/her caregiver to report any drug-induced ADRs such as nausea, sexual dysfunction, fatigue, dizziness, myalgia, arthralgia, numbness/tingling sensation on extremities, hypotension, reflex tachycardia, bradycardia, imbalance or improper muscles coordination and reduce urinary output.

URINARY ANTISEPTICS

Conditions affecting the urinary tract and bladder are quite common in clinical practice. These conditions include urinary tract infections, bladder spasms, bladder pain, and benign prostatic hyperplasia (BPH).

Drugs acting on urinary bladder, urethra and prostate are mentioned in Figure 10.2.

The following group of people are vulnerable to UTIs:

- Females, due to shorter perineal area and short urethra.
- Patients with indwelling catheters or intermittent catheterizations often develop bladder infections or cystitis, which can result from bacteria introduced into the bladder by these devices.

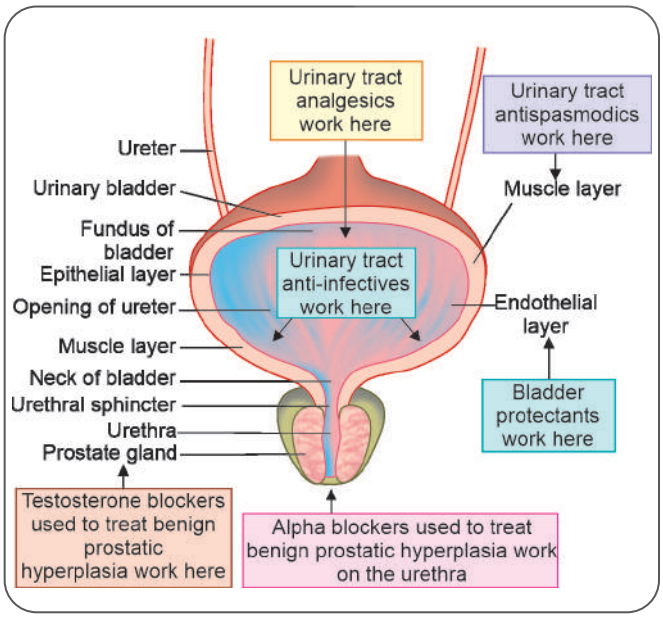


Fig. 10.2: Drugs acting on urinary bladder, urethra and prostate

- Blockage anywhere in the urinary tract can lead to backflow problems and the spread of bladder infections into the kidney (pyelonephritis).
- Patients with anatomical abnormalities of urinary tract.

The signs and symptoms of urinary tract infection include: Increased frequency of micturition, urgency, burning micturition (associated with cystitis), chills, fever, flank pain, and tenderness (associated with acute pyelonephritis).

To treat these infections, clinicians use specific urinary tract anti-infectives, which include antibiotics, as well as some specific agents that alter the urinary pH.

The orally administered antimicrobial agents (AMAs), which attain good antibacterial concentration only in urine, with little or no systemic antibacterial effects are called *urinary antiseptics*. This is equivalent to a form of local therapy. These drugs are excreted unchanged *via* renal route and are useful mainly in lower urinary tract infections. Examples: nitrofurantoin, nalidixic acid and methenamine, etc.

Some other drugs, which are also useful in treating urinary tract infections, are known as urinary anti-infectives drugs.

Urinary tract anti-infectives are:

The antibiotics used specifically to treat urinary tract infections are as follows:

- Nalidixic acid and cinoxacin, nitrofurantoin (urinary antiseptics), methenamine (hexamine), phenazopyridine
  - Fluoroquinolones: Norfloxacin, ofloxacin, ciprofloxacin, prulifloxacin, etc.
  - Cephalosporins: Cefixime, cefuroxime, ceftriaxone, ceftazidime, etc.
  - Aminoglycosides: Amikacin, gentamicin, etc.
  - Penicillin's: Ampicillin, amoxicillin, piperacillin, ticarcillin, etc.
  - Sulphonamide: Cotrimoxazole, etc.
  - Tetracyclines, fosfomycin, etc.

Drugs Used in Urinary Tract Infections

Nalidixic Acid and Cinoxacin

- They belong to quinolones, but did not achieve systemic antibacterial levels; therefore, only indicated for the treatment of lower UTI, which are caused by gram negative microorganisms.
- Well absorbed orally with bioavailability of 80–95%.
- Quinolones inhibits the DNA gyrase and topoisomerase IV.
- They are widely distributed in body fluids and tissues with plasma t½ is 3–10 hours.
- Poor oral absorption is observed due to presence of divalent cations and excreted *via* kidney.
- The side effects are rashes, drowsiness, headache, GI upset (nausea, vomiting and abdominal pain), seizures in children, photosensitivity, urticaria and fever.
- They are absolutely contraindicated in infants.

Nitrofurantoin

- It is bacteriostatic agent shown its high-efficacy in low/acidic pH.
- Many microorganisms show their resistance toward nitrofurantoin such as proteus and pseudomonas aeruginosa species.
- It is only used in UTI which is associated with *E. coli* infection as second-line agent.

Mechanism of Action

It causes rapid intracellular conversion into highly reactive intermediates by bacterial reductase. This intermediate then reacts nonspecifically with many ribosomal proteins and disrupts synthesis of proteins, RNA, DNA and metabolic processes.

- It is well absorbed orally and rapidly metabolized in liver and excreted through kidneys.
- Patients with who is on probenecid drug therapy and azotemia, the use of nitrofurantoin should be restricted as it reduces the renal tubular secretion and may lead to serious side effects.
- In case of UTI due to *E. coli*, nitrofurantoin is given in a dose of 50–100 mg thrice daily (5–7 mg/kg/day) for 5–10 days and for suppression of long-term management of chronic lower UTI 50 mg twice daily or 100 mg at bed time.

Indications

- Uncomplicated lower urinary tract infection.
- Suppressive long-term treatment of chronic lower UTI.
- Recurrent cystitis in women.
- Prophylaxis of urinary tract infection (catheterization/instrumentation of the lower urinary tract).

Side Effects

- **Most common:** GI upset (nausea, epigastric pain, and diarrhea, brown discoloration of urine.
- **Acute reaction:** Malaise, leucopenia.
- **Chronic:** Pulmonary fibrosis, hepatotoxicity.
- **Long-term:** Peripheral neuritis, G6PD deficiency.
- Nitrofurantoin is absolutely contraindicated in neonates, pregnant women and in patients with poor renal function.

Methenamine (Hexamine)

- It is hexamethylenetetramine, a prodrug.
- This drug needs acidic pH below 5.5 to make it decomposed in acidic medium and form formaldehyde which is responsible for antibacterial activity.
- It does not have any systemic antimicrobial effect.
- Acidification of urine can be made by combining methenamine with mandelic and hippuric acid.
- As this drug easily decomposed in GIT, to protect them, enteric-coated tablet is given orally.
- Methenamine is not advocated in acute UTI but can be useful in chronic and/or resistant UTIs.
- It is given in a dose of 1 g thrice/four times in a day with fluid restriction.
- Side effects is mainly due to formation of formaldehyde, which is usually associated with gastritis, hematuria and chemical cystitis.

Phenazopyridine

- It is a urinary analgesic.
- This is a dye, used in UTI for its analgesic properties.
- It does not have antimicrobial activity.
- It is used in a dose of 200–400 mg trice daily for dysuria, burning sensation and urgency (in cystitis).
- The most common side effect is GI upset, like epigastric pain and nausea.
- These drugs are preferred in the treatment of urinary tract infections but used for treating other infections also.

- In complicated urinary tract infections and pyelonephritis, drugs are used mainly in injectable form to achieve good bioavailability and early minimum inhibitory concentration for attaining maximum efficacy and early response.
- *The above list of drugs is for empirical use only and the specific urinary tract infections treatment should be based upon urine culture sensitivity report only.*

Table 10.5 gives the antimicrobial treatment of urinary tract infections.

Factors Affecting AMAs for Managing UTIs

Urinary pH

- Urine pH plays pivotal role for the action of antimicrobial agents.
- *Many drugs effective only in acidic media, e.g., tetracyclines, nitrofurantoin, cloxacillin and methenamine and in alkaline*

Table 10.5: Antimicrobial treatment of urinary tract infections

Drugs	Special points
Sulfonamides	• Sulfamethoxazole is used in combination with trimethoprim. • The combination is used in chronic urinary tract infection, streptococcal pharyngitis and gum infection.
Cotrimoxazole	• Fixed dose combination of sulfamethoxazole (sulfonamide) and trimethoprim. • Sulfonamide inhibits folate synthase and trimethoprim inhibits dihydrofolate reductase and produce supra-additive effect. • Urinary tract infections: specially for chronic or recurrent cases or in prostatitis, because trimethoprim is concentrated in prostate. • Usually given in undiagnosed UTI which is commonly caused by Chlamydia trachomatis. • It is not indicated in UTI in pregnancy. • It can be given in women with cystitis and catheter induced UTI.
Quinolones	• First-generation quinolones such norfloxacin and ciprofloxacin are still very efficacious for management of UTIs. • As these drugs act against gram negative microorganism, also used in resistant cases of UTI. • In case of chronic UTI resistant to ampicillin or cotrimoxazole, norfloxacin has been given for 12 weeks. • FQ are absolutely contraindicated in pregnancy.
Penicillin group of drugs	• Ampicillin or amoxicillin were the first-line drugs for treating UTI, but due to emergence of drug resistance by *E. coli*, the use of these agent is restricted. • Parenteral amoxicillin + clavulanic acid with gentamycin is used for initial management of pyelonephritis. • Many newer penicillins, like cloxacillin is not helpful for treating UTI due to development of drug resistance. • In chronic urinary such as renal calculi and hypertrophy of prostate with indwelling catheter, piperacillin or ticarcillin are used.
Cephalosporins	• Cephalosporins should be started after antimicrobial isolation. • Cephalosporins are advocated in Proteus and nosocomial Klebsiella infection in females. • Cephalosporins are used for empiric treatment of community acquired UTI. • In case of recurrent cystitis in a woman who wish to get pregnant, prophylaxis of cephalexin is indicated as an alternative therapy.
Gentamicin	• Gentamicin should be started after antimicrobial isolation. • It should be used cautiously, as it follows narrow margin of safety. • Gentamycin is very effective against UTI including Pseudomonas. • Combination of amoxicillin with clavulanic acid and gentamycin is used to treat acute pyelonephritis.
Chloramphenicol	• Chloramphenicol should not be used commonly, as this agent associated with serious side effects. • It is used as reserved drugs in case of pyelonephritis, where other drugs are less effective/resistant.
Tetracyclines	• Nowadays, use of tetracyclines is not recommended due to emergence of resistance. • It is used only after proven bacterial culture studies in case of cystitis caused by Chlamydia trachomatis infection.
Fosfomycin	• It inhibits bacterial cell wall synthesis in a very early stage. • It is effective against both gram-positive and gram-negative microorganisms. • It is used in combination with aminoglycosides, FQs and β-lactam antibiotics to synergies their antibacterial activity. • Indicated in uncomplicated lower urinary tract infections in a dose of 3 g single dose regimen.

media, e.g., cephalosporins, gentamicin, fluoroquinolones and cotrimoxazole.

- Acidification is not possible in urease positive proteus infection; therefore, it is advised to treat this type of infection with a drug that act in high pH.

Renal Impairment

- In patient with derange kidney profile, treatment of UTI is very difficult.
- Many drugs that are used to treat UTI is contraindicated, e.g., cephalosporins, tetracycline (except doxycycline) and Methenamine.
- Use of some drugs, like, nalidixic acid, aminoglycosides and nitrofurantoin are not indicated because these agents are associated with further renal damage.
- Bacteriology profiling and use of narrow spectrum antibiotics are recommended for patients with poor renal function.

Prophylaxis for Urinary Tract Infection

- Prophylaxis is given to prevent the infection in immunocompromised individuals such as:
  - Patients with prolong history of catheterization or instrumentation who are prone to develop bacterial infection.
  - Patients with indwelling catheters.
  - Congenital urinary tract defects which are uncorrectable.
  - Recurrent cystitis in a female with reproductive age group.
  - Chronic obstruction in urinary tract leads to stasis of urine (prostatic hypertrophy).
- The recommended drugs for prophylaxis are given once daily regimen preferably at bed time, these includes *nitrofurantoin 100 mg, cephalexin 250 mg, cotrimoxazole 480 mg and norfloxacin 400 mg.*

CHOLINERGIC AND ANTICHOLINERGIC DRUGS USED IN URINARY SYSTEM

Cholinergic Drugs (Cholinomimetic, Parasympathomimetic)

The drugs which produce acetylcholine-like actions on different organ systems are known as cholinergic drugs. These drugs act either by directly interacting with cholinergic receptors or by increasing availability of acetylcholine (ACh) at these sites. Drugs acting directly on cholinergic receptors are known as cholinergic agonists (e.g., Bethanechol) and the drugs which increase availability of ACh by inhibiting cholinesterase enzyme are known as anticholinesterases (e.g., Neostigmine).

Cholinergic Receptors

There are two types of cholinergic receptors: *Muscarinic and nicotinic.*

1. **Muscarinic receptors** have been divided into 5 subtypes M_1, M_2, M_3, M_4 and M_5. These are located on heart, blood vessels, eye, smooth muscles and glands of gastrointestinal, respiratory and urinary tracts, sweat glands, etc.

   In the urinary system, the cholinergic drugs act through M_3 receptors. These have a role in visceral smooth muscle contraction and glandular secretions. Some of the actions are also mediated through M_2 receptors.

   Smooth muscles in ureter and detrusor muscle in urinary bladder are contracted through M_3 receptors. Peristalsis in ureter is increased. The detrusor muscle contracts while the bladder trigone and sphincter relax which leads to micturition.
2. **Nicotinic receptors** are present at skeletal muscle end plate and autonomic ganglia.

Must Know

Cholinergic drugs useful in urinary system: *Bethanechol and Neostigmine*

Acetylcholine is not used clinically due to nonselective and extremely short duration of action.

- **Bethanechol:** It initiates micturition by increasing the tone of detrusor muscle. It is indicated in postoperative/postpartum nonobstructive urinary retention and neurogenic bladder.

  It is given in a dose of 10–50 mg orally and 2.5–5 mg subcutaneously. Commonly seen side effects are abdominal cramps, involuntary urination and defecation, vasodilation, sweating, hypotension and may precipitate asthma, etc.
- **Neostigmine:** Neostigmine is an anticholinesterase and given in a dose of 0.5–1 mg subcutaneously in cases of postoperative urinary retention. It should not be given in the cases of organic obstruction in the urinary tract.

Anticholinergic Drugs

(Muscarinic receptor antagonists, Atropine, Parasympatholytic)

The drugs which block actions of ACh on autonomic effectors are known as *anticholinergic drugs*. The effects are exerted through antagonism at the level of muscarinic receptors.

The anticholinergic drugs useful for urinary system disorders are:

- **General antispasmodics:** Dicyclomine, valethamate.
- **Drugs acting specifically on urinary system [Vesicoselective drugs]:** Oxybutynin, flavoxate, tolterodine, darifenacin and solifenacin.

Mechanism of Action

- The anticholinergic drugs have a relaxant effect on all the visceral smooth muscles that receive parasympathetic motor innervations.
- Anticholinergic drugs have relaxant action on ureter and urinary bladder. Clinically, this effect is beneficial in increasing bladder capacity by decreasing the tone of detrusor muscles.
- This also controls detrusor hyperreflexia in patients suffering from neurogenic bladder or enuresis.

General Antispasmodics

(Dicyclomine, Valethamate)

- **Dicyclomine:** In addition to weak anticholinergic effects, it also has direct smooth muscle relaxant action. It is used in renal colic in a dose of 10–20 mg oral/IM for adults and 5–10 mg for children.
- **Valethamate:** It is useful as antispasmodic in a variety of colic's such as urinary, biliary and intestinal colic. Primarily, it is used, as a smooth muscle relaxant to hasten dilatation of cervix during delivery. It is given in a dose of 8 mg IM and 10 mg orally BD.

Must Know

Drotaverine

- It is an effective *nonanticholinergic spasmolytic drug*. It causes smooth muscle relaxation by inhibiting phosphodiesterase-4 (PDE-4) enzyme.
- It is used both orally and parenterally for intestinal, biliary and renal colics, irritable bowel syndrome, uterine spasms, etc.
- It is given in a dose of 40–80 mg BD/TDS orally and 20–40 mg IM BD/TDS.

Drugs Acting Specifically on Urinary System (Vesicoselective Drugs)

(Oxybutynin, flavoxate, tolterodine, darifenacin and solifenacin)

- **Oxybutynin:** It has selective action on bladder and is useful in patients suffering from vesical spasm, urinary frequency, neurogenic bladder and nocturnal enuresis. It is given in a dose of 5 mg BD/TDS orally in adults and 2.5 mg BD in children above 5 years.
- **Flavoxate** is prescribed in urinary frequency, urgency and dysuria associated with lower urinary tract infection. It is given in a dose of 200 mg TDS.
- **Tolterodine:** It is M_3 selective muscarinic antagonist with specific action on urinary bladder. The anticholinergic side effects are less. It is prescribed in overactive bladder with urinary frequency and urgency. It is given in a dose of 1–2 mg BD or 2–4 mg OD orally.
- **Darifenacin** and **solifenacin** are other relatively M_3 subtype selective antimuscarinics useful in bladder disorders.

ACIDIFIERS AND ALKALINIZERS

Acidifiers and alkalinizes are the agents, which are used or can be used to acidify or alkalinize the urine, respectively as per requirement. As these agents are given systemically, they temporarily alter the pH of blood also, may it be for a short duration only as the compensatory mechanisms of the body immediately respond and maintain the normal pH of blood and other body fluids.

Certain AMAs act better in acidic urine, while others work better in alkaline urine. However, specific intervention to produce urine of desired pH is rarely required because most of the drugs used in UTI attain high concentration in urine and minor changes in urinary pH do not affect clinical outcome. In case of inadequate response or in complicated cases, measurement of urinary pH and appropriate corrective measure may help.

Must Know

The AMAs which work better in acidic pH are: Nitrofurantoin, tetracyclines, cloxacillin, etc.

The AMAs which work better in alkaline pH are: Cephalosporins, fluoroquinolones, aminoglycosides, cotrimoxazole, etc.

Acidifiers

- These are the drugs, which are used or can be used to acidify urine whenever required for therapeutic purpose.
- Renal excretion of basic drugs (e.g., amphetamine) can be enhanced by acidification of urine.
- Ammonium chloride, potassium chloride and ascorbic acid can be used for this purpose. Rarely required practically.

Alkalinizers

- These are the drugs, which are used or can be used to alkalinize urine whenever required for therapeutic purpose.
- Renal excretion of acidic drugs (e.g., salicylates) can be enhanced by acidification of urine.
- Potassium citrate, magnesium citrate, sodium citrate and tricitrate solutions of these compounds can be used for this purpose.

Mechanism of Action of Alkalinizes

After oral administration, these agents are absorbed systemically and increase the plasma bicarbonate levels; *blood pH is raised*. In case of patients suffering from acidosis, the excess hydrogen ions are buffered and the clinical manifestations of acidosis are reversed.

These agents are metabolized to bicarbonates, which are excreted as free bicarbonate ions in the urine and increase the urinary pH. These make the urine alkaline and help in dissolution of uric acid and cystine stone.

Pharmacokinetics

- These agents are given orally in tablet form or solution form. After oral administration, these are absorbed systemically and converted to sodium and potassium bicarbonates.
- These are excreted *via* renal route in the form of bicarbonates. <5% is excreted in unchanged form.
- These agents have had quick onset of action within 1 hour of administration and remains up to 12 hours.
- Alkalinizes when given in a dose of 10–15 mL QID: maintain a urine pH of 6.5–7.4 and when given in a dose of 15–20 mL QID maintain a urine pH of 7.0–7.6.

The alkalinizing effect remains up to 24 hours after the last dose.

Indications

- To treat UTIs along with AMAs, which work better in alkaline urine.
- To treat the symptoms of systemic acidosis for shorter durations. Higher doses are needed for this purpose.
- For prevention and treatment of uric acid and calcium oxalate stones.
- For symptomatic improvement in burning micturition in case of cystitis and urethritis.
- To enhance the excretion of acidic drugs (phenobarbitone, salicylates) in case of poisonings. Intravenous soda bicarbonate is used. It can be tried but only when renal functions are not compromised. It is rarely practiced now.

NURSING IMPLICATIONS

Patients Receiving Urinary Antiseptics, Acidifiers and Alkalinizers

Assessment	Nursing diagnosis
Baseline Assessment • Obtain complete medical and personal history related to the diseases prior to admission. That includes history of cerebrovascular, cardiovascular, respiratory, metabolic disease, drug history, drug/food allergy, OTC/herbal drugs, and present prescription. • Assess for contraindications or cautions: Known allergies to these drugs to avoid hypersensitivity reactions. • Assess any infectious sign and symptoms, fever, swelling, abscess, pain. • Assess patients-related laboratory investigations such as CBC with PS, bacterial culture and microscopy, LFT and RFT. • Obtain appropriated baseline of vital signs, urinary output, cardiac output, bowel sound, height and weight. • Assess any sign of bleeding, and patient or caregiver ability to understand instruction.	• Infection • Pain • Hyperthermia • Fatigue • Poor knowledge about medicines • Drug-related side effects, diarrhea, fever, fluid overload

Contd...

Assessment	Nursing diagnosis

Assessment During Drug Administration

- During drug administration nurses should monitor patients' hemodynamic status.
- Also monitor the therapeutic effect of drugs such as improvement in fever, reduced sign and symptoms of infection/UTIs.
- Always give test dose intradermally before injecting therapeutic dose to prevent drug-induced hypersensitivity.
- Emergency drug tray should always be ready for immediately handling of the reactions.
- Ensure that culture and sensitivity tests are performed before therapy begins and are repeated if the response is not as expected to ensure appropriate treatment of the infection.
- Frequently monitor the patients CBC, urinalysis, bacterial culture and sensitivity, liver and kidney test profile.
- It is highly important to observe any side effects, such as skin rashes, nausea, vomiting, diarrhea, dizziness, photosensitivity, abdominal cramp, reduce urine output during drug administration and should be reported promptly.

Patient-related goals and outcomes

- The patients:
  - Will observe the therapeutic outcome of given drugs, like resolution of UTI and relief of signs and symptoms and feeling of wellbeing.
  - Can have negligible drug-induced side effects.
  - Can express the indications, side effects and precaution of given drugs.
  - Can self-administer drug in prescribed dose and timing.

Nursing interventions	Patient-centered care

To Ensure Drug Therapeutic Effect

- It is mandatory to observe patient frequently for any drug-induced effect. Patients' hemodynamic status should be maintained in a normal level as set by the physician.
- Monitor patient response to the drug (resolution of UTI and relief of signs and symptoms); repeat culture and sensitivity tests as recommended for evaluation of the effectiveness of all these drugs.
- Continue monitoring of the desire therapeutic effects, like reduction in pain, fever, infectious symptoms of bacteremia.
- Catheter care should be properly done and nurse should keep a record of the exact date of catheterization, as catheter needs to be changed within 2–3 weeks.
- Provide or assist with perineal hygiene as indicated to reduce the risk of reinfection or prevent transmission of infection.
- Evaluate the effectiveness of the teaching plan (patient can name drug, dosage, adverse effects to watch for, specific measures to avoid them, and measures to take to increase the effectiveness of the drug).
- Supportive measures should be provided by nursing staff, that improves the patient's compliance and better outcome.
- Follow and teach appropriate technique of routes of administration.

Minimize Side Effects

- If any sign of anaphylaxis is noticed after the injection, the treatment of the reaction should be started immediately and it should be informed immediately to senior and physician. Continue monitor till 2 weeks even after completion of antimicrobial therapy.

- Patient should be educated about the importance and proper technique of urine sample collection. Midstream urine should be collected in the sterile container.
- Encourage the patient to drink lots of fluids (unless contraindicated by other conditions) to promote flushing of the bladder and prevent urinary stasis and to avoid citrus juices and antacids, which promote alkaline urine and provide opportunity for bacteria growth.
- Patient should be educated not to withdraw drug even after feeling better; increased risk of developing antibiotics resistance. Take the full course of antibiotics and don't share the drugs with anyone even family members.
- Provide thorough patient teaching, including drug name, prescribed dose, measures for avoidance of adverse effects, and warning signs that may indicate possible problems.
- Instruct the patient if fever is persisted for 3 days even after taking antibiotics, should report treating physician immediately.
- Educate patient and his/her caregiver to report any unwanted side effect, such as rashes, syncope, wheezing, angioedema, pruritus, flushing, urticaria, dizziness and breathing difficulties; these could be sign and symptoms of anaphylaxis.

Contd...

Nursing interventions	Patient-centered care
• The previous history of allergy to different penicillin must be taken carefully before administering penicillin injections. • Patients should be informed beforehand that ampicillin can cause diarrhea. • Periodically monitor the laboratory investigations such as liver and kidney profile, bacterial culture and sensitivity, urinalysis, CBC. • Closely monitor any sign of superinfections (fungal/yeast infection) in patient with comorbidities. • Monitor patient's pulse, ECG and electrolyte as penicillin can cause hypernatremia and hyperkalemia. • Monitor any earing problem as aminoglycoside is very toxic to ear and patient should be warned for not driving or operating the machinery. • Monitor if patient has any sign of photosensitivity, ototoxicity; may associated with tetracyclines and vancomycin side effects. • Monitor the vision of the patient regularly as linezolid is associated with optic neuropathy. • Frequently monitor any side effect induced by tetracyclines (especially in children); tetracyclines have chelating property with calcium phosphate, selectively enter the teeth and growing bone of the fetus and children. This causes hypoplasia of dental enamel with pitting, cusp malformation, yellow/brown pigmentation and increased susceptibility to caries. • Monitor patient's urine output as demeclocycline can cause diabetes insipidus by antagonizing antidiuretic hormone (ADH) action. • The renal functions should be regularly monitored during co-trimoxazole therapy. • Take extra precaution in women taking OCP; penicillins reduce the effectiveness of OCPs. • Monitor any drugs-induced ADRs, like GI upset (abdominal pain, nausea, vomiting), rashes, fatigue, headache, dizziness, blood dyscrasias.	• Advise patient to take plenty of liquids and also take precautionary yogurt or buttermilk or pre and probiotics to avoid incidence of diarrhea. • Advise patient and his/her caregiver to report any drug-induced side effects, i.e., GI upset (abdominal pain, nausea, vomiting), rashes, fatigue, headache, drowsiness, dyspnea, dizziness, blood dyscrasias.

SEXUALLY TRANSMITTED DISEASES

- In view of emergence of antimicrobial resistance, the selection of antibiotics is utmost important for the treatment in sexually transmitted disease (STDs).
- The following criteria should be met for the treatment of STDs (Table 10.6), and the drug should be:
  - Economical
  - Highly efficacious
  - Should be advisable in pregnancy and lactation
  - Single and preferably oral administrable dose
  - Less incidence of adverse drugs profile
  - Less incidence drug resistance

Table 10.6: Treatment of STDs-associated syndromes (WHO recommendations)

STDs causing organism	First-line drug regimen	Second-line drug regimen
Gonococcal infections		
Uncomplicated anogenital infection	• Ciprofloxacin 500 mg orally (single dose) Or • Azithromycin, 2 g orally (single dose) Or • Ceftriaxone, 125 mg IM injection (single dose) Or • Cefixime, 400 mg (single dose) Or • Spectinomycin, 2 g IM injection (single dose)	• Kanamycin, 2 g by IM injection (single dose) Or • Trimethoprim (80 mg)/sulfamethoxazole (400 mg), 10 tablets orally, as a single dose daily for 3 days.
Disseminated infection	• Ceftriaxone, 1 g IV or IM injection, OD for 7 days, Or • Spectinomycin, 2 g IM injection, BD for 7 days.	–
Gonococcal ophthalmia		
Adult gonococcal conjunctivitis	• Ceftriaxone, 125 mg IM injection (single dose) Or • Spectinomycin, 2 g IM injection (single dose) Or • Ciprofloxacin, 500 mg orally, (single dose)	Kanamycin, 2 g IM injection (single dose).
Neonatal gonococcal conjunctivitis	• Ceftriaxone, 50 mg/kg IM injection (single dose), to a maximum of 125 mg	• Kanamycin 25 mg/kg IM injection (single dose), to a maximum of 75 mg, Or • Spectinomycin, 25 mg/kg IM injection (single dose), to a maximum of 75 mg.
Infants born to mothers with gonococcal infection	Ceftriaxone 50 mg/kg IM injection (single dose), to a maximum of 125 mg.	• Kanamycin 25 mg/kg by IM injection (single dose), to a maximum of 75 mg, Or • Spectinomycin, 25 mg/kg IM injection (single dose), to a maximum of 75 mg.
Chlamydia trachomatis infections (nonlymphogranuloma venereum)		
Uncomplicated urethral, endocervical or rectal infections	• Doxycycline, 100 mg orally, BD for 7 days Or • Azithromycin, 1 g orally (single dose)	• Amoxycillin, 500 mg orally, TDS for 7 days • Erythromycin, 500 mg orally, QID for 7 days, Or • Ofloxacin, 300 mg orally, BD for 7 days Or • Tetracycline, 500 mg orally, QID for 7 days.
Chlamydial infection in pregnancy	• Erythromycin, 500 mg orally QID for 7 days, Or • Amoxycillin, 500 mg orally, TDS for 7 days.	–
Neonatal chlamydial conjunctivitis	Erythromycin syrup, 50 mg/kg/day orally, in 4 divided doses for 14 days	Trimethoprim 40 mg with sulfamethoxazole 200 mg orally, BD for 14 days.
Infantile pneumonia	• Erythromycin syrup, 50 mg/kg/day for 14 days. • If not available, trimethoprim 40 mg with sulfamethoxazole 200 mg may be given orally BD for 3 weeks.	–
Lymphogranuloma venereum	• Doxycycline, 100 mg orally, BD for 14 days Or • Erythromycin, 500 mg orally, QID for 14 days.	• Tetracycline, 500 mg orally, QID for 14 days.
Syphilis		
Early syphilis	Benzathine benzylpenicillin 2.4 million IU, by IM injection, at a single session.	• Procaine benzylpenicillin, 1.2 million IU daily, by IM injection, for 10 consecutive days. • For penicillin-allergic (non-pregnant patients) ▪ Doxycycline, 100 mg orally, BD for 15 days Or ▪ Tetracycline, 500 mg orally, QID for 15 days
Late latent syphilis	Benzathine benzylpenicillin, 2.4 million IU by IM injection, once weekly for 3 consecutive weeks.	• Procaine benzylpenicillin, 1.2 million IU, by IM injection, once daily for 20 consecutive days. • For penicillin-allergic non-pregnant patients ▪ Doxycycline, 100 mg orally, BD for 30 days Or ▪ Tetracycline, 500 mg orally, QID for 30 days.

Contd...

STDs causing organism	First-line drug regimen	Second-line drug regimen
Neurosyphilis	Aqueous benzylpenicillin, 12–24 million IU by IV injection, administered daily in doses of 2–4 million IU QID for 14 days.	• Procaine benzylpenicillin, 1.2 million IU by IM injection, OD, and probenecid, 500 mg orally QID, both for l0–14 days. • For penicillin-allergic nonpregnant patients ▪ Doxycycline, 200 mg orally, BD for 30 days, Or ▪ Tetracycline, 500 mg orally, QID for 30 days
Syphilis in pregnancy	Benzathine benzylpenicillin 2.4 million IU, by IM injection, at a single session.	• For penicillin-allergic pregnant patients: ▪ Early syphilis • Erythromycin, 500 mg orally, QID for 15 days ▪ Late syphilis • Erythromycin, 500 mg orally, QID for 30 days
Congenital syphilis		
Early congenital syphilis (<2 years of age) and Infants with abnormal cerebrospinal fluid	• Aqueous benzylpenicillin 100,000–150,000 IU/kg/day administered as 50000 IU/kg/dose IV every 12 hours, during the first 7 days of life and every 8 hours thereafter for a total of 10 days. Or • Procaine benzylpenicillin, 50000 IU/kg by IM injection, OD for 10 days.	—
Congenital syphilis (>2 years)	• Aqueous benzylpenicillin, 200000–300000 IU/kg/day by IV or IM injection, administered as 50000 IU/kg every 4–6 hours for 10–14 days.	• For penicillin-allergic patients, after the first month of life: ▪ Erythromycin, 7.5–12.5 mg/kg orally, QID for 30 days.
Chancroid	• Ciprofloxacin, 500 mg orally, BD for 3 days Or • Erythromycin base, 500 mg orally, QID for 7 days Or • Azithromycin, 1 g orally (single dose).	Ceftriaxone, 250 mg by IM injection (Single dose)
Granuloma inguinale (donovanosis)	• Azithromycin, 1 g orally on first day, then 500 mg orally once a day, Or • Doxycycline, 100 mg orally, BD.	• Erythromycin, 500 mg orally, QID, Or • Tetracycline, 500 mg orally, QID, Or • Trimethoprim (80 mg)/sulfamethoxazole (400 mg), 2 tablets orally, BD for a minimum of 14 days
Genital herpes infections		
First clinical episode	• Acyclovir, 200 mg orally, 5 times daily for 7 days Or • Acyclovir, 400 mg orally, TDS for 7 days Or • Famciclovir, 250 mg, TDS for 7 days Or • Valaciclovir, 1 g, BD for 7 days	—
Recurrent infections	• Acyclovir, 200 mg orally, 5 times daily for 7 days Or • Acyclovir, 400 mg orally, TDS for 5 days Or • Acyclovir, 800 mg orally, TDS for 5 days Or • Famciclovir 125 mg orally BD for 5 days Or • Valaciclovir 500 mg orally BD for 5 days Or • Valaciclovir 1000 mg orally OD for 5 days	—
Suppressive therapy	• Acyclovir, 400 mg orally, BD, continuously Or • Famciclovir 250 mg orally BD Or • Valaciclovir 500 mg orally OD Or • Valaciclovir 1000 mg orally OD	—
Herpes in pregnancy	• Acyclovir, 400 mg orally	—
Neonates	• Acyclovir, 10 mg/kg IV, TDS for 10–21 days	—
Herpes and HIV coinfection	• Acyclovir 400 mg orally 3–5 times daily until clinical resolution is attained	—

Contd...

STDs causing organism	First-line drug regimen	Second-line drug regimen
Venereal warts	• Podofilox 0.5% solution or gel twice daily for 3 days, followed by 4 days of no treatment, and the cycle repeated up to 4 times. (Total volume of podofilox should not exceed 0.5 mL/day) • Imiquimod 5% cream applied with a finger at bedtime, left on overnight, 3 times a week for as long as 16 weeks. (The treatment area should be washed with soap and water 6–10 hours after application)	—
Trichomonas vaginalis infections	• Metronidazole, 2 g orally, in a single dose Or • Tinidazole, 2 g orally, in a single dose	• Metronidazole, 400 or 500 mg orally, BD for 7 days Or • Tinidazole, 500 mg orally, BD for 5 days
Candidiasis	• Miconazole or clotrimazole, 200 mg intravaginally, daily for 3 days Or • Clotrimazole, 500 mg intravaginally, as a single dose Or • Fluconazole, 150 mg orally, as a single dose.	Nystatin, 100,000 IU intravaginally, daily for 14 days

STUDENT ASSIGNMENT

LONG ANSWER QUESTIONS

1. What are diuretic agents? Classify them and describe loop diuretics.
2. Describe the complications of diuretic therapy.
3. Describe the rationale of combination of potassium-sparing diuretic with loop diuretics.
4. Describe the diuretics that are used as therapy for hypertension.

SHORT ANSWER QUESTIONS

1. Why are the loop diuretics called high-ceiling diuretics?
2. Why is mannitol used in head injury?
3. Write short notes on:
   a. Urinary antiseptics
   b. Bethanechol
   c. Alkalinizes
   d. Furosemide
   e. Spironolactone

MULTIPLE CHOICE QUESTIONS

1. Eplerenone:
   a. Is an aldosterone antagonist
   b. Can cause hyperkalemia in predisposed patients
   c. Is a diuretic
   d. All of the above

2. The drug that can be used for producing alkalinization of urine is:
   a. Hydrochlorothiazide
   b. Furosemide
   c. Acetazolamide
   d. Spironolactone

3. Desmopressin can be used for all of the following conditions; except:
   a. Neurogenic diabetes insipidus
   b. Nephrogenic diabetes insipidus
   c. Bedwetting in children
   d. Bleeding due to hemophilia

4. The drug causing gynecomastia is:
   a. Spironolactone
   b. Rifampicin
   c. Penicillin
   d. Bumetanide

5. Hypercalcemia is caused by which of the following drug?
   a. Bumetanide
   b. Spironolactone
   c. Thiazide
   d. Furosemide

6. In diabetes insipidus, diuretic showing paradoxical antidiuretic activity is:
   a. Thiazide
   b. Triamterene
   c. Spironolactone
   d. Furosemide

7. High-ceiling diuretics are useful in the treatment of all of the following conditions; except:
   a. Generalized edema
   b. Cerebral edema
   c. Acute pulmonary edema
   d. Pulmonary hypertension

8. The site of action of the loop diuretic furosemide is:
   a. Thick ascending limb of loop of Henle
   b. Descending limb of loop of Henle
   c. Proximal tubule
   d. Distal tubule

9. Thiazides can cause:

a. Hyperkalemic paralysis
b. Hypouricemia
c. Hypolipidemia
d. Impotence

10. Thiazides diuretics causes all; except:

a. Hyperglycemia
b. Increased calcium excretion
c. Useful in congestive heart failure
d. Decreased uric acid excretion

11. Mannitol is not useful for:

a. Glaucoma
b. Raised ICT
c. Impending renal failure
d. Pulmonary edema

12. Potassium-sparing diuretics act on:

a. Na^+K^+ pump
b. Aldosterone receptor
c. Carbonic anhydrase
d. Na^+ Cl^- symporter

13. Loop diuretics act by:

a. Inhibition of Na^+–Cl^- Symport
b. Inhibition of Na^+–K^+–2 Cl^- cotransport
c. Inhibition of Na^+–K^+ ATPase
d. Inhibition of H^+–K^+ ATPase
e. Inhibition of renal epithelial Na^+ channel

14. Which of the following is an aldosterone antagonist?

a. Eplerenone
b. Amiloride
c. Triamterene
d. All of the above

15. Loop diuretics act on:

a. PCT
b. DCT
c. Thick ascending loop of Henle
d. Collecting duct

ANSWER KEY

1. d	**2.** c	**3.** b	**4.** a	**5.** d	**6.** a	**7.** d	**8.** a
9. d	**10.** b	**11.** d	**12.** b	**13.** b	**14.** a	**15.** c	

Textbook of

Pharmacology for BSc Nursing Students

Salient Features

Learning Objectives given in the beginning of each chapter enable the student to know what he/she will learn after reading.

LEARNING OBJECTIVES

After studying the chapter, readers will be able to:

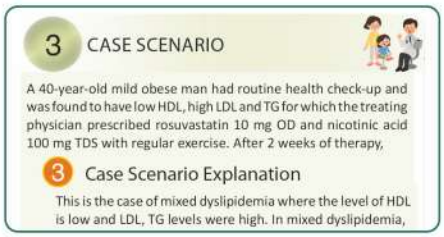
- Describe the principles of pharmacodynamics, pharmacokinetics, classification, and the principles of drug administration.
- Understand the effects of microsomal enzymes.
- Classify the types of drug formulations.

Every chapter begins with a **Chapter Outline** to provide a glimpse of the content discussed.

CHAPTER OUTLINE

- Introduction
- Definitions
- Sources of Drugs
- Systems of Measurement
- Terminology Used

Each and every topic has been introduced with **Clinical Case Scenario** along with its explanation from theoretical and clinical integration point of view.



Important information that needs attention has been highlighted in **Must Know** boxes.

Must Know

Additive Drug Combinations

- Aspirin + paracetamol as analgesic/antipyretic
- Amlodipine + atenolol as antihypertensive
- Glibenclamide + metformin as hypoglycemic

Numerous **Figures** are used to make learning easy for students.

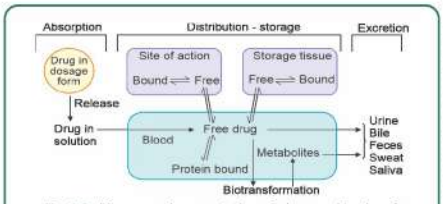


Fig. 1.2: Diagrammatic presentation of pharmacokinetics of a drug

Various **Tables** are used to help students grasp the concepts quickly.

Table 8.16: Dose and duration of tinidazole in various indications

Indications	Dose and duration
Intestinal amoebiasis	2 g OD for 3 days (children 30–50 mg/kg/day) or 0.6 g BD for 5–10 days
Amoebic liver abscess	2 g daily for 3–6 days
Trichomoniasis and giardiasis	2 g single dose or 0.6 g OD for 7 days

Nursing Implications enlist the various measures required by nurses while administering the drugs of every class.

NURSING IMPLICATIONS

Nursing Implications for Histamines

Administer the drug apart from any other oral medications approximately 1 hour before or 2-hour after to ensure adequate absorption of the other medications.

Drug-to-drug interactions have been given separately to help the nurses during their practice.

DRUG INTERACTIONS

- The levels of digoxin and warfarin are increased by amiodarone by reducing their renal clearance.
- Amiodarone can produce additive A-V block, if given along with calcium channel blockers or β-blockers.

Detailed **Student Assignment** in the form of exercises in each and every chapter will facilitate structured learning and revision of the material provided in the respective chapters.

STUDENT ASSIGNMENT

LONG ANSWER QUESTIONS

1. What is a drug? Describe the various sources of drugs.
2. Explain the various routes of drug administration.

SHORT ANSWER QUESTIONS

1. Write short notes on:
   a. Pharmacokinetics
   b. Pharmacodynamics

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