



INTRODUCTION

- **Diuretic** – agent that increases urine volume
- **Natriuretic** – agent that increases urinary sodium excretion
- **Aquaretic** – agent that increases excretion of solute free water

PRINCIPLES OF DIURETIC EFFECTS

- Interference with Na^+ reabsorption at one nephron site interferes with other renal functions linked to it
- Increased flow and Na^+ delivery to distal nephron stimulates K^+ (and H^+) secretion
- Diuretics act only if Na^+ reaches their site of action. The magnitude of the diuretic effect depends on the amount of Na^+ reaching that site
- Diuretic actions at different nephron sites can produce synergism

All, EXCEPT **spironolactone**, act from the luminal side of the tubular cellular membrane

RENAL TUBULE TRANSPORT MECHANISMS

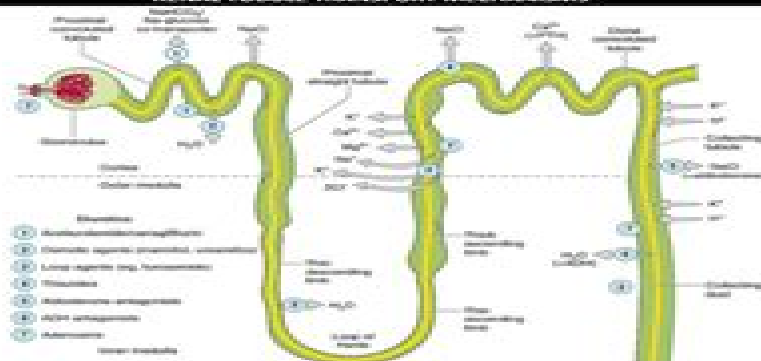


FIGURE 15-1 Tubule transport systems and sites of action of diuretics. ACE, angiotensin-converting enzyme; PTH, parathyroid hormone.

Proximal Convoluted Tubule

- Reabsorbs Na^+ (66%), NaHCO_3 (85%), K^+ (65%), glucose, amino acid & water (50%)
 - Potassium reabsorbed via paracellular pathway
 - Water reabsorbed passively maintaining osmolality in nearly constant level
 - **Na^+/H^+ exchanger (NHE3)** – it initiates the reabsorption of NaHCO_3
 - **Sodium-glucose cotransporter, isoform 2 (SGLT2)** – is responsible for reabsorbing much of the glucose that is filtered by the glomeruli
- Inhibitors of SGLT2 have been approved to treat **diabetes mellitus**.
- **Carbonic anhydrase inhibitors** – blocks NaHCO_3 reabsorption
 - **Adenosine receptor antagonist** – blocks NaCl reabsorption

Loop of Henle

- Pumps Na^+ , K^+ & Cl^- out of the lumen into the interstitium
- Provides the concentration gradient for the countercurrent concentrating mechanism
- **Thick ascending limb (TAL)** – it is the **diluting segment**

It follows the thin limb of Henle's loop, actively **reabsorbs NaCl** from the lumen (about 25% of the filtered sodium), but unlike the proximal tubule and the thin descending limb of Henle's loop, it is nearly **impermeable to water**

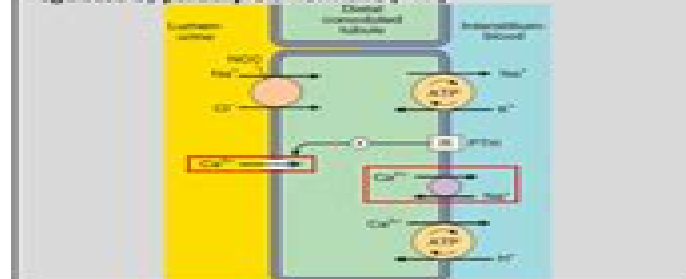
Salt reabsorption in the TAL therefore **DILUTES** the tubular fluid. Medullary portions of the TAL contribute to medullary hypertonicity and thereby also play an important role in concentration of urine by the collecting duct

- **$\text{Na}^+/\text{K}^+/\text{2Cl}^-$ cotransporter** (called **NKCC2** or **NKCC1**) – is the NaCl transport system in the luminal membrane of the TAL
- Secondary reabsorption of Ca^{2+} and Mg^{2+} also happens here

Distal Convoluted Tubule

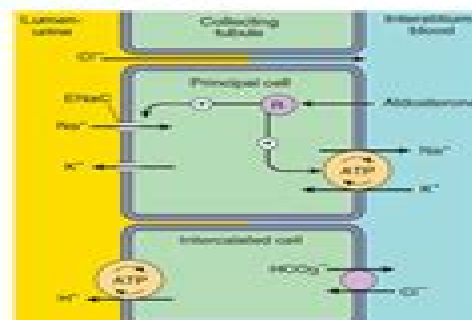
- Actively pumps Na^+ & Cl^- out of the lumen nephron
- 10% Na reabsorbed
- Impermeable to water
- NaCl reabsorption further dilutes the tubular fluid
- **Na^+/Cl^- cotransporter (NCC)** – is the NaCl transport in the DCT
- Ca^{2+} reabsorption

Ca^{2+} is actively reabsorbed by the DCT epithelial cell via an apical Ca^{2+} channel and basolateral $\text{Na}^+/\text{Ca}^{2+}$ exchanger. This is regulated by **parathyroid hormone (PTH)**



Collecting Tubule

- 2-5% NaCl reabsorption
- Final site of NaCl reabsorption
- Determines the final Na^+ concentration of the urine
- Tight regulator of body fluid volume
- Influenced by mineralocorticoids
- Important site of K^+ secretion



Principal Cells

- Major sites of Na^+ , K^+ , and water transport system
- Do not contain apical cotransport system for Na^+ and other ions
- Exhibits separate ion channels for Na^+ and K^+

Intercalated Cells (α & β)

- Primary sites of H^+ (α cells) or HCO_3^- (β cells) secretion



Renal Pharmacology

**National Institutes of Health (U.S.).
Division of Research Grants**



Renal Pharmacology:

Insights in Renal Pharmacology: 2021 Giuseppe Remuzzi, Matthew Griffin, Norberto Perico, 2022-10-18 Renal Pharmacology James William Fisher, 1971 Papers presented at a renal pharmacology conference in the Dept of Pharmacology Tulane University School of Medicine in New Orleans La Jan 13 1970 held in connection with the joint meetings of the U S Public Health Service Pharmacology A and Medicine B Study Sections *Renal Pharmacology* Manuel Martinez-Maldonado, 2013-06-29 Frequently attempts to design experiments utilizing the methodology described in articles in trade journals can be frustrating Description of procedures because of space constraints are not always complete The present volume attempts to bring together in one reference source many of the techniques which are utilized in the study of the kidney It provides a thorough compendium of research tools framed by the critical analysis of the theoretical background of renal physiology biochemistry and pharmacology discussed in Volume 4A Some areas previously dealt with are not covered from a methodological point of view since adequate information does exist elsewhere e g methods of whole kidney ATPase isolation Since drugs acting on the kidney may alter not only functional but anatomical integrity a chapter on the preparation of tissue for morphological studies has been included The important developments in analysis of minute ultramicro quantities of tissue and biological fluids as well as methodological advances in studies of the isolated kidney are thoroughly covered It is my hope that investigators research fellows and graduate students will benefit from the information contained in this volume and that together with its companion tome it will be a ready reference for the renal physiologist the renal pharmacologist and the nephrologist The contributors have provided painstaking descriptions and when required mathematical analyses of the techniques described herein I wish to thank all of them for their enthusiasm and the excellence of their contributions **Cardio-renal and Cell Pharmacology** Hiroshi Yoshida, 1982 **Kidney Disease and Nephrology Index**, 1977 *New Insights Into Renal Fibrosis and Therapeutic Effects of Natural Products* Dan-Qian Chen, Zhiyong Guo, 2022-05-30 **Library of Congress Subject Headings** Library of Congress, 2010 Library of Congress Subject Headings Library of Congress. Cataloging Policy and Support Office, 2003 Library of Congress Subject Headings Library of Congress. Office for Subject Cataloging Policy, 1992 Research Awards Index, 1980 **Research Grants Index** National Institutes of Health (U.S.). Division of Research Grants, 1975 **Pediatric Critical Care E-Book** Jerry J. Zimmerman, 2016-11-29 Still the 1 resource for today's pediatric ICU teams Pediatric Critical Care 5th Edition covers the entire field from basic science to cutting edge clinical applications Drs Bradley P Fuhrman and Jerry J Zimmerman accompanied by an expert team of editors and contributors from around the world bring you today's best information on the current and future landscape of pediatric critical care so you can consistently deliver optimum care to your young patients Boasts highly readable concise chapters with hundreds of useful photos diagrams algorithms and clinical pearls Clear logical organ system approach allows you to focus on the development function and treatment of a wide range of disease entities

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- Chapter 1: Introduction to Renal Pharmacology
- Chapter 2: Essential Elements of Renal Pharmacology
- Chapter 3: Renal Pharmacology in Everyday Life
- Chapter 4: Renal Pharmacology in Specific Contexts
- Chapter 5: Conclusion

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Table of Contents Renal Pharmacology

1. Understanding the eBook Renal Pharmacology

- The Rise of Digital Reading Renal Pharmacology
- Advantages of eBooks Over Traditional Books
- 2. Identifying Renal Pharmacology
 - Exploring Different Genres
 - Considering Fiction vs. Non-Fiction
 - Determining Your Reading Goals
- 3. Choosing the Right eBook Platform
 - Popular eBook Platforms
 - Features to Look for in an Renal Pharmacology
 - User-Friendly Interface
- 4. Exploring eBook Recommendations from Renal Pharmacology
 - Personalized Recommendations
 - Renal Pharmacology User Reviews and Ratings
 - Renal Pharmacology and Bestseller Lists
- 5. Accessing Renal Pharmacology Free and Paid eBooks
 - Renal Pharmacology Public Domain eBooks
 - Renal Pharmacology eBook Subscription Services
 - Renal Pharmacology Budget-Friendly Options
- 6. Navigating Renal Pharmacology eBook Formats
 - ePub, PDF, MOBI, and More
 - Renal Pharmacology Compatibility with Devices
 - Renal Pharmacology Enhanced eBook Features
- 7. Enhancing Your Reading Experience
 - Adjustable Fonts and Text Sizes of Renal Pharmacology
 - Highlighting and Note-Taking Renal Pharmacology
 - Interactive Elements Renal Pharmacology
- 8. Staying Engaged with Renal Pharmacology
 - Joining Online Reading Communities
 - Participating in Virtual Book Clubs
 - Following Authors and Publishers Renal Pharmacology

9. Balancing eBooks and Physical Books Renal Pharmacology
 - Benefits of a Digital Library
 - Creating a Diverse Reading Collection Renal Pharmacology
10. Overcoming Reading Challenges
 - Dealing with Digital Eye Strain
 - Minimizing Distractions
 - Managing Screen Time
11. Cultivating a Reading Routine Renal Pharmacology
 - Setting Reading Goals Renal Pharmacology
 - Carving Out Dedicated Reading Time
12. Sourcing Reliable Information of Renal Pharmacology
 - Fact-Checking eBook Content of Renal Pharmacology
 - Distinguishing Credible Sources
13. Promoting Lifelong Learning
 - Utilizing eBooks for Skill Development
 - Exploring Educational eBooks
14. Embracing eBook Trends
 - Integration of Multimedia Elements
 - Interactive and Gamified eBooks

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