Renal Mechanism

Renin Release

- Renin release is triggered by:
  - Reduced stretch of the granular JG cells
  - Stimulation of the JG cells by activated macula densa cells
  - Direct stimulation of the JG cells via β_1-adrenergic receptors by renal nerves
  - Angiotensin II

Renin Release

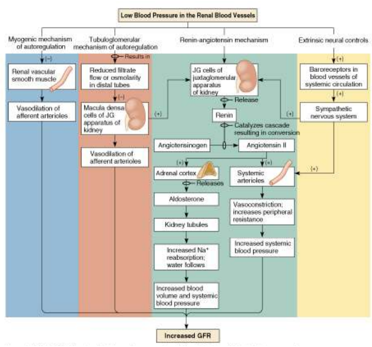

Figure 24.11

Other Factors Affecting Glomerular Filtration

- Prostaglandins (PGE_2 and PGI_2)
  - Vasodilators produced in response to sympathetic stimulation and angiotensin II
  - Are thought to prevent renal damage when peripheral resistance is increased
- Nitric oxide – vasodilator produced by the vascular endothelium
- Adenosine – vasoconstrictor on renal vasculature
- Endothelin – a powerful vasoconstrictor secreted by tubule cells and the vascular endothelium

Tubular Reabsorption

- A transepithelial process whereby most tubule contents are returned to the blood
- Transported substances move through three membranes
  - Luminal and basolateral membranes of tubule cells
  - Endothelium of peritubular capillaries
- Only Ca^{2+}, Mg^{2+}, K^+, and some Na^+ are reabsorbed via paracellular pathways

Tubular Reabsorption

- All organic nutrients are reabsorbed
- Water and ion reabsorption is hormonally controlled
- Reabsorption may be an active (requires ATP) or passive process

Sodium Reabsorption: Primary Active Transport

- Sodium reabsorption is almost always by active transport
  - Na^+ enters the tubule cells at the luminal membrane
  - Na^+ is actively transported out of the tubules by a Na^+-K^+ ATPase pump
- From there it moves to peritubular capillaries, due to:
  - Low hydrostatic pressure
  - High osmotic pressure of the blood
- Na^+ reabsorption provides the energy and the means for reabsorbing most other solutes

Reabsorption by PCT Cells

- Active pumping of Na^+ drives reabsorption of:
  - Water by osmosis
  - Anions and fat-soluble substances by diffusion
  - Organic nutrients and selected cations by secondary active transport

Reabsorption by PCT Cells

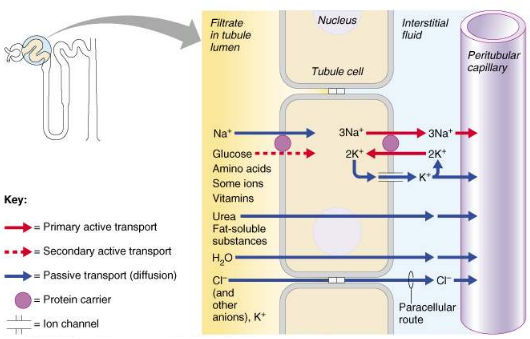

Figure 24.12

Nonreabsorbed Substances

- A transport maximum (T_m):
  - Reflects the number of carriers in the renal tubules available
  - Exists for nearly every substance that is actively reabsorbed
- When the carriers are saturated, excess of that substance is excreted

Nonreabsorbed Substances

- Substances are not reabsorbed if they:
  - Lack carriers
  - Are not lipid soluble
  - Are too large to pass through membrane pores
- Urea, creatinine, and uric acid are the most important nonreabsorbed substances

Absorptive Capabilities of Renal Tubules and Collecting Ducts

- Substances reabsorbed in PCT include:
  - Sodium, all nutrients, cations, anions, and water
  - Urea and lipid-soluble solutes
  - Small proteins
- Loop of Henle
  - H_2O, Na^+, Cl^-, K^+ (descending)
  - Ca^{2+}, Mg^{2+}, and Na^+ (ascending)

Absorptive Capabilities of Renal Tubules and Collecting Ducts

- DCT
  - Ca^{2+}, Na^+, H^+, K^+, and water
  - HCO_3^- and Cl^-
- Collecting duct
  - Water and urea

Na^+ Entry into Tubule Cells

- Passive entry – Na^+-K^+ ATPase pump
- In the PCT – facilitated diffusion using symport and antiport carriers
- In the ascending loop of Henle – facilitated diffusion via Na^+-K^+-$2Cl^-$ symport system
- In the DCT – Na^+-Cl^- symporter
- In collecting tubules – diffusion through membrane pores

Na^+ Entry into Tubule Cells

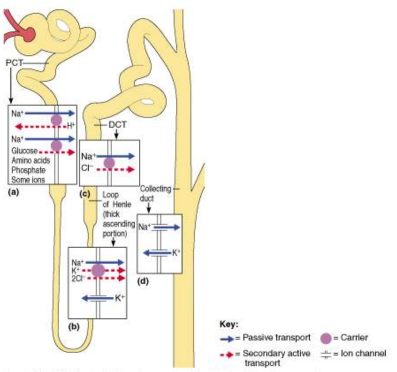

Figure 24.13

Tubular Secretion

- Essentially reabsorption in reverse, where substances move from peritubular capillaries or tubule cells into filtrate
- Tubular secretion is important for:
  - Disposing of substances not already in the filtrate
  - Eliminating undesirable substances such as urea and uric acid
  - Ridding the body of excess potassium ions
  - Controlling blood pH

Regulation of Urine Concentration and Volume

- Osmolality
  - The number of solute particles dissolved in 1L of water
  - Reflects the solution's ability to cause osmosis
- Body fluids are measured in milliosmols (mOsm)
- The kidneys keep the solute load of body fluids constant at about 300 mOsm
  - This is accomplished by the countercurrent mechanism

Countercurrent Mechanism

- By the time the filtrate reaches the loop of Henle, the amount and flow are reduced by 65% but it is still isosmotic
- The solute concentration in the loop of Henle ranges from 300 mOsm to 1200 mOsm
- The loop of Henle functions as a countercurrent multiplier
- Dissipation of the medullary osmotic gradient is prevented because the blood in the vasa recta equilibrates with the interstitial fluid

Loop of Henle: Countercurrent Multiplier

- The descending loop of Henle:
  - Is relatively impermeable to solutes
  - Is permeable to water
- The ascending loop of Henle:
  - Is impermeable to water
  - Actively transports sodium chloride into the surrounding interstitial fluid

Loop of Henle: Countercurrent Multiplier

- Collecting ducts in the deep medullary regions are permeable to urea
- The vasa recta is a countercurrent exchanger that:
  - Maintains the osmotic gradient
  - Delivers nutrient blood supply to the cells in the area

Loop of Henle: Countercurrent Multiplier

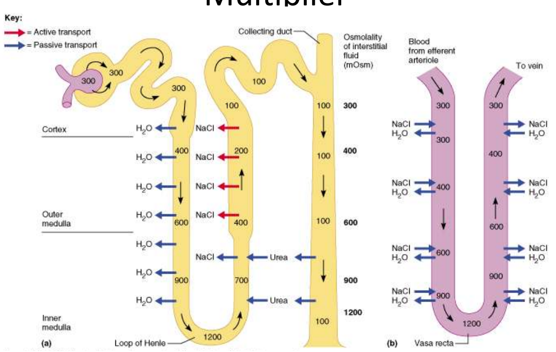

Figure 24.14

Formation of Dilute Urine

- Filtrate is diluted in the ascending loop of Henle
- Dilute urine is created by allowing this filtrate to continue into the renal pelvis
- This will happen as long as antidiuretic hormone (ADH) is *not* being secreted
- Collecting ducts remain impermeable to water; no further water reabsorption occurs
- Sodium and selected ions can be removed by active and passive mechanisms
- Urine osmolality can be as low as 50 mOsm (one-sixth that of plasma)

Formation of Concentrated Urine

- Antidiuretic hormone (ADH) inhibits diuresis
- This equalizes the osmolality of the filtrate and the interstitial fluid
- In the presence of ADH, 99% of the water in filtrate is reabsorbed
- ADH-dependent water reabsorption is called *facultative water reabsorption*
- ADH is the signal to produce concentrated urine
- The kidneys' ability to respond depends upon the high medullary osmotic gradient

Formation of Concentrated Urine

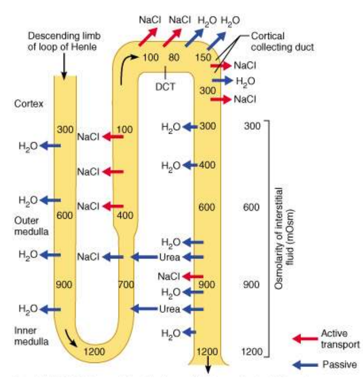

Figure 24.15

Diuretics

- Chemicals that enhance the urinary output include:
  - Any substance not reabsorbed
  - Substances that exceed the ability of the renal tubules to reabsorb it
- Osmotic diuretics include:
  - High glucose levels – carries water out with the glucose
  - Alcohol – inhibits the release of ADH
  - Caffeine and most diuretic drugs – inhibit sodium ion reabsorption
  - Lasix – inhibits Na^+-K^+-$2Cl^-$ symporters

Renal Clearance

- The volume of plasma that is cleared of a particular substance in a given time
- Renal clearance tests are used to:
  - Determine the GFR
  - Detect glomerular damage
  - Follow the progress of diagnosed renal disease

$$RC = UV/P$$

RC = renal clearance rate
U = concentration (mg/ml) of the substance in urine
V = flow rate of urine formation (ml/min)
P = concentration of the same substance in plasma

Physical Characteristics of Urine

- Color and transparency
  - Clear, pale to deep yellow (due to urochrome)
  - Concentrated urine has a deeper yellow color
  - Drugs, vitamin supplements, and diet can change the color of urine
  - Cloudy urine may indicate infection of the urinary tract

Physical Characteristics of Urine

- Odor
  - Fresh urine is slightly aromatic
  - Standing urine develops an ammonia odor
  - Some drugs and vegetables (asparagus) alter the usual odor

Physical Characteristics of Urine

- pH
  - Slightly acidic (pH 6) with a range of 4.5 to 8.0
  - Diet can alter pH
- Specific gravity
  - Ranges from 1.001 to 1.035
  - Dependent on solute concentration

Chemical Characteristics of Urine

- Urine is 95% water and 5% solutes
- Nitrogenous wastes include urea, uric acid, and creatinine
- Other normal solutes include:
  - Sodium, potassium, phosphate, and sulfate ions
  - Calcium, magnesium, and bicarbonate ions
- Abnormally high concentrations of any urinary constituents may indicate pathology
- Disease states alter urine composition dramatically

Ureters

- Slender tubes that convey urine from the kidneys to the bladder
- Ureters enter the base of the bladder through the posterior wall
  - This closes their distal ends as bladder pressure increases and prevents backflow of urine into the ureters

Ureters

- Ureters have a trilayered wall
  - Transitional epithelial mucosa
  - Smooth muscle mucosa
  - Fibrous connective tissue adventitia
- Ureters actively propel urine to the bladder via response to smooth muscle stretch

Urinary Bladder

- Smooth, collapsible, muscular sac that temporarily stores urine
- It lies retroperitoneally on the pelvic floor posterior to the pubic symphysis
  - Males – prostate gland surrounds the neck inferiorly
  - Females – anterior to the vagina and uterus
- Trigone – triangular area outlined by the openings for the ureters and the urethra
  - Clinically important because infections tend to persist in this region

Urinary Bladder

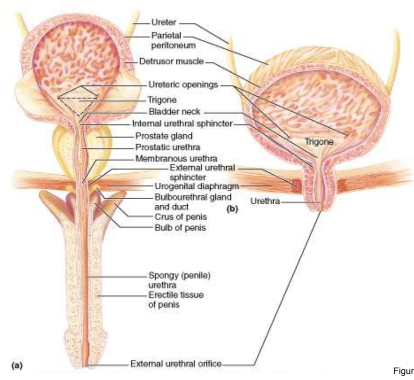

Figure 24.18a, b

Urinary Bladder

- The bladder wall has three layers
  - Transitional epithelial mucosa
  - A thick muscular layer
  - A fibrous adventitia
- The bladder is distensible and collapses when empty
- As urine accumulates, the bladder expands without significant rise in internal pressure