Physiology of Urinary system

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3rd Year/ Lecture 2

Urine Formation I: Glomerular Filtration

- kidneys convert blood plasma to urine in three stages
  - **glomerular filtration**
  - **tubular reabsorption and secretion**
  - **water conservation**
- **glomerular filtrate** – the fluid in the capsular space
  - similar to blood plasma except that is has almost no protein
- **tubular fluid** – fluid from the proximal convoluted tubule through the distal convoluted tubule
  - substances have been removed or added by tubular cells
- **urine** – fluid that enters the collecting duct
  - undergoes little alteration beyond this point except for changes in water content

Structure of Glomerulus

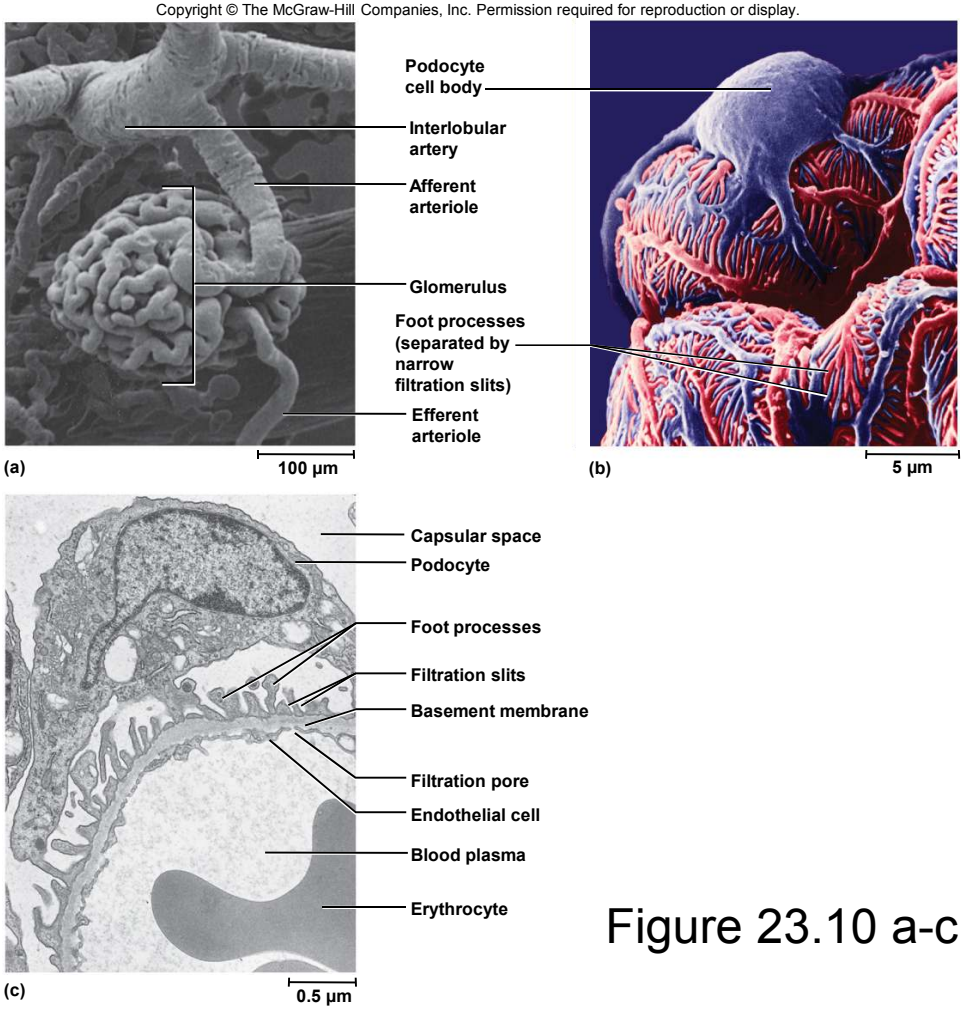


Figure 23.10 a-c

Filtration Pores and Slits

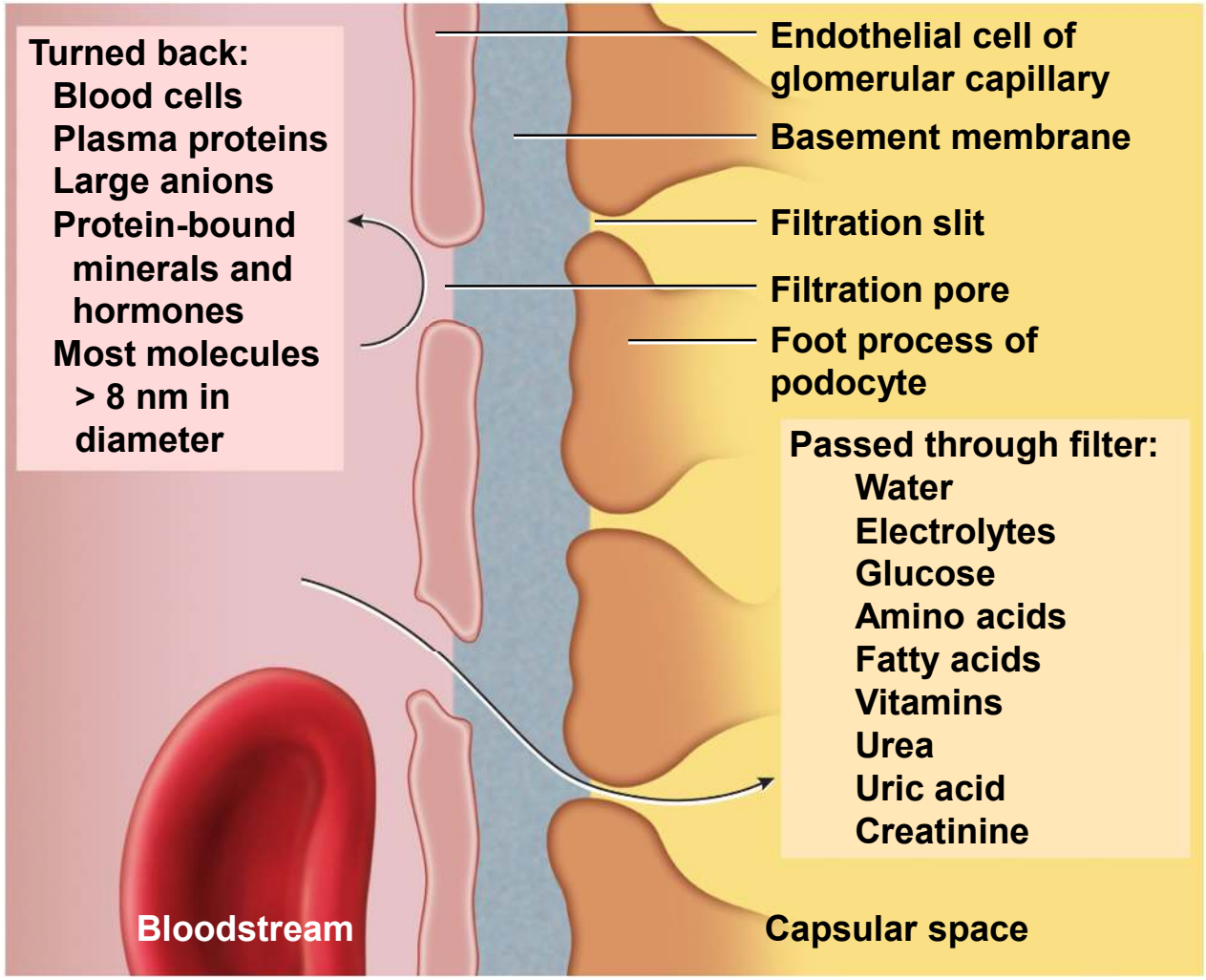


Figure 23.11

Filtration Membrane

- **glomerular filtration** – a special case of the capillary fluid exchange process in which water and some solutes in the blood plasma pass from the capillaries of the glomerulus into the capsular space of the nephron
- **filtration membrane** – three barriers through which fluid passes
  - **fenestrated endothelium of glomerular capillaries**
    - 70-90 nm filtration pores exclude blood cells
    - highly permeable
  - **basement membrane**
    - proteoglycan gel, negative charge, excludes molecules greater than 8nm
    - albumin repelled by negative charge
    - blood plasma is 7% protein, the filtrate is only 0.03% protein
  - **filtration slits**
    - **podocyte** cell extensions (**pedicels**) wrap around the capillaries to form a barrier layer with 30 nm filtration slits
    - negatively charged which is an additional obstacle for large anions

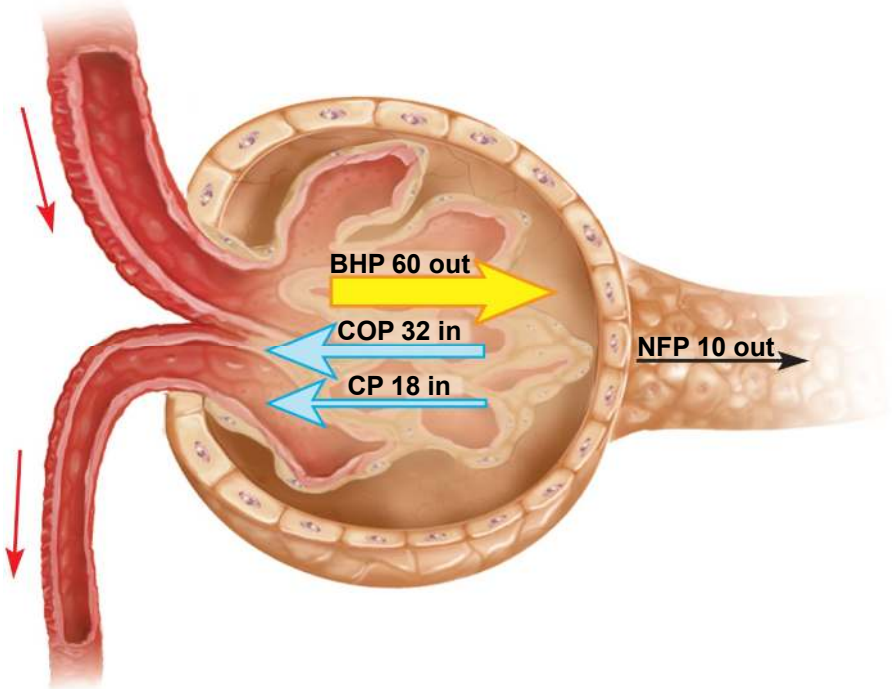
Filtration Membrane

- almost any molecule smaller than 3 nm can pass freely through the filtration membrane
  - water, electrolytes, glucose, fatty acids, amino acids, nitrogenous wastes, and vitamins
- some substances of low molecular weight are bound to the plasma proteins and cannot get through the membrane
  - most calcium, iron, and thyroid hormone
    - unbound fraction passes freely into the filtrate
- **kidney infections and trauma** can damage the filtration membrane and allow albumin or blood cells to filter.
  - **proteinuria (albuminuria)** – presence of protein in the urine
  - **hematuria** – presence of blood in the urine
- distance runners and swimmers often experience temporary proteinuria or hematuria
  - prolonged, strenuous exercise greatly reduces profusion of kidney
  - glomerulus deteriorates under prolonged hypoxia

Filtration Pressure

- **blood hydrostatic pressure** (BHP)
  - much higher in glomerular capillaries (60 mm Hg compared to 10 to 15 in most other capillaries)
  - because afferent arteriole is larger than efferent arteriole
  - larger inlet and smaller outlet
- **hydrostatic pressure** in capsular space
  - 18 mm Hg due to high filtration rate and continual accumulation of fluid in the capsule
- **colloid osmotic pressure (COP) of blood**
  - about the same here as elsewhere - 32 mm Hg
  - glomerular filtrate is almost protein-free and has no significant COP
- **higher outward pressure of 60 mm Hg**, opposed by two inward pressures of 18 mm Hg and 32 mm Hg
- **net filtration pressure** - $60_{out} - 18_{in} - 32_{in} =$ **10 mm Hg_{out}**

Filtration Pressure



Blood hydrostatic pressure (BHP)	**60 mm Hg_{out}**
Colloid osmotic pressure (COP)	**–32 mm Hg_{in}**
Capsular pressure (CP)	**–18 mm Hg_{in}**
Net filtration pressure (NFP)	**10 mm Hg_{out}**

Figure 23.12

high BP in glomerulus makes kidneys vulnerable to hypertension

it can lead to rupture of glomerular capillaries, produce scarring of the kidneys (nephrosclerosis), and atherosclerosis of renal blood vessels, ultimately leading to renal failure

Glomerular Filtration Rate (GFR)

- **glomerular filtration rate** (GFR) – the amount of filtrate formed per minute by the 2 kidneys combined
  - GFR = NFP x K_f ≈125 mL / min or 180 L / day, male
  - GFR = NFP x K_f ≈105 mL / min or 150 L / day, female
    - net filtration pressure (NFP)
    - filtration coefficient (K_f) depends on permeability and surface area of filtration barrier
- total amount of filtrate produced equals 50 to 60 times the amount of blood in the body
  - 99% of filtrate is reabsorbed since only 1 to 2 liters urine excreted / day

Regulation of Glomerular Filtration

- **GFR too high**
  - fluid flows through the renal tubules too rapidly for them to reabsorb the usual amount of water and solutes
  - urine output rises
  - chance of dehydration and electrolyte depletion
- **GFR too low**
  - wastes reabsorbed
  - azotemia may occur
- **GFR controlled** by adjusting **glomerular blood pressure** from moment to moment
- **GFR control is achieved by three homeostatic mechanisms**
  - renal autoregulation
  - sympathetic control
  - hormonal control

Renal Autoregulation of GFR

- **renal autoregulation –** the ability of the nephrons to adjust their own blood flow and GFR without external (nervous or hormonal) control
- enables them to maintain a relatively stable GFR in spite of changes in systemic arterial blood pressure
- two methods of autoregulation: **myogenic mechanism** and **tubuloglomerular feedback**
- **myogenic mechanism** – based on the tendency of smooth muscle to contract when stretched
  - increased arterial blood pressure stretches the afferent arteriole
  - arteriole constricts and prevents blood flow into the glomerulus from changing much
  - when blood pressure falls
  - the afferent arteriole relaxes
  - allows blood flow more easily into glomerulus
  - filtration remains stable

Renal Autoregulation of GFR

- **tubuloglomerular feedback** – mechanism by which glomerulus receives feedback on the status of the downstream tubular fluid and adjust filtration to regulate the composition of the fluid, stabilize its own performance, and compensate for fluctuation in systemic blood pressure
  - **juxtaglomerular apparatus** – complex structure found at the very end of the nephron loop where it has just reentered the renal cortex
  - loop comes into contact with the afferent and efferent arterioles at the vascular pole of the renal corpuscle

Renal Autoregulation of GFR

- **three special kind of cells** occur in the juxtaglomerular apparatus:
  - **macula densa** – patch of slender, closely spaced epithelial cells at end of the nephron loop on the side of the tubules facing the arterioles
    - senses variations in flow or fluid composition and secretes a paracrine that stimulates JG cells
  - **juxtaglomerular (JG) cells** – enlarged smooth muscle cells in the afferent arteriole directly across from macula densa
    - when stimulated by the macula
    - they dilate or constrict the arterioles
    - they also contain granules of renin, which they secrete in response to drop in blood pressure
  - **mesangial cells** – in the cleft between the afferent and efferent arterioles and among the capillaries of the glomerulus
    - connected to macula densa and JG cells by gap junctions and communicate by means of paracrines
    - build supportive matrix for glomerulus, constrict or relax capillaries to regulate flow

Juxtaglomerular Apparatus

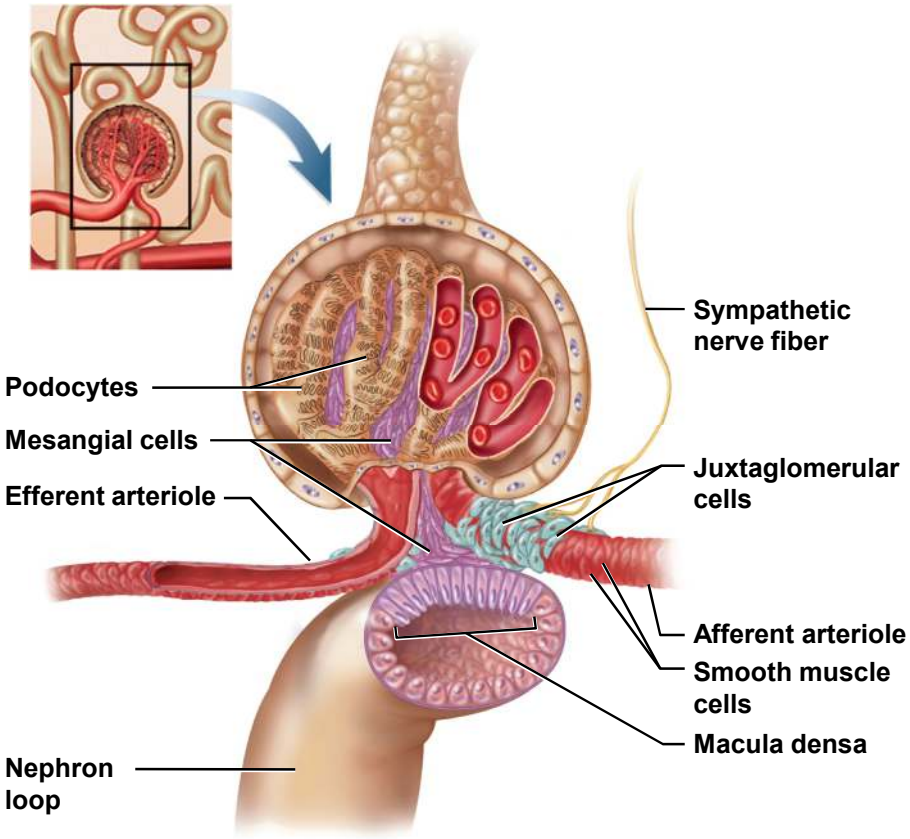


Figure 23.13

- **if GFR rises**
  - the flow of tubular fluid increases and more NaCl is reabsorbed
  - macula densa stimulates JG cells with a paracrine
  - JG cells contract which constricts afferent arteriole, reducing GFR to normal OR
  - mesangial cells may contract, constricting the capillaries and reducing filtration
- **if GFR falls**
  - macula relaxes afferent arterioles and mesangial cells
  - blood flow increases and GFR rises back to normal.

Effectiveness of Autoregulation

- maintains a dynamic equilibrium - GFR fluctuates within narrow limits only
  - blood pressure changes do affect GFR and urine output somewhat
- renal autoregulation can not compensate for extreme blood pressure variation
  - over a MAP range of 90 – 180 mm Hg, the GFR remains quite stable
  - below 70 mm Hg, glomerular filtration and urine output cease
  - occurs in hypovolemic shock

Negative Feedback Control of GFR

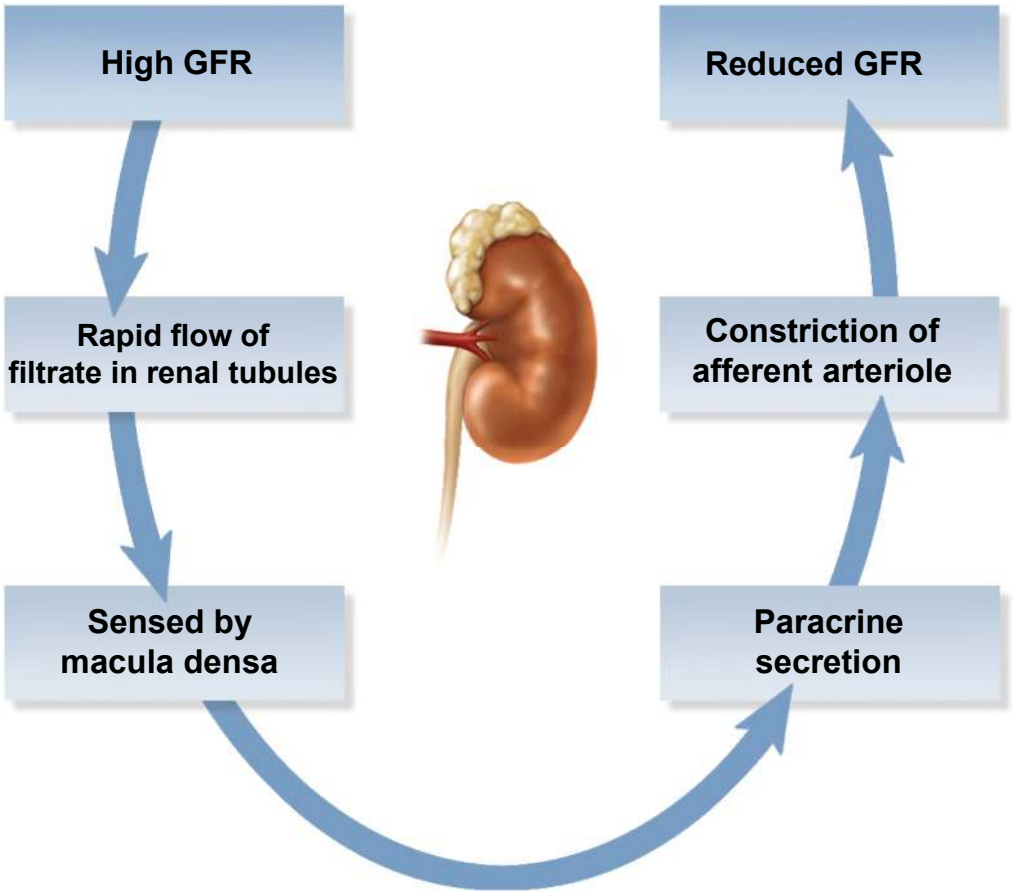


Figure 23.14

Sympathetic Control of GFR

- sympathetic nerve fibers richly innervate the renal blood vessels
- sympathetic nervous system and adrenal epinephrine **constrict the afferent arterioles** in strenuous exercise or acute conditions like circulatory shock
  - reduces GFR and urine output
  - redirects blood from the kidneys to the heart, brain, and skeletal muscles
  - GFR may be as low as a few milliliters per minute

Renin-Angiotensin-Aldosterone Mechanism

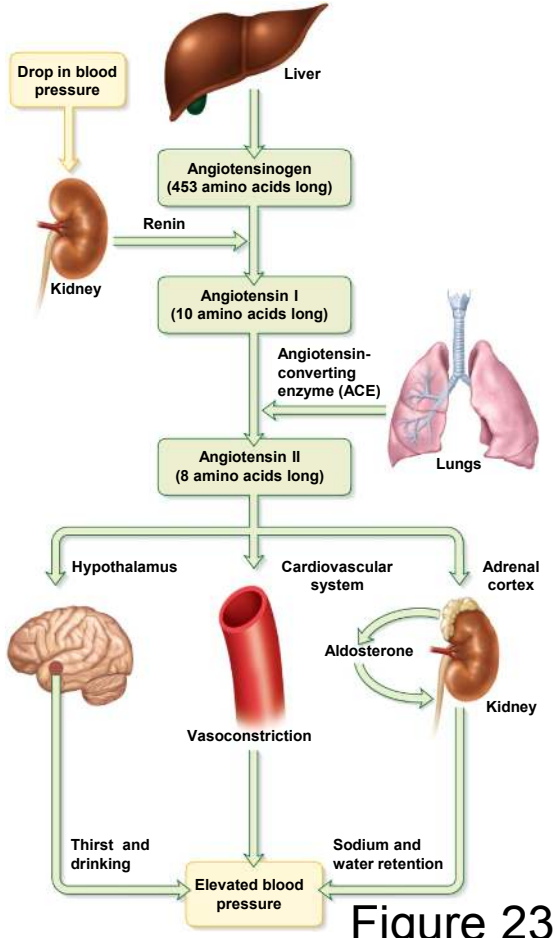


Figure 23.15

- ***renin*** secreted by juxtaglomerular cells if BP drops dramatically
- renin converts **angiotensinogen**, a blood protein, into **angiotensin I**
- in the **lungs and kidneys**, **angiotensin-converting enzyme (ACE)** converts angiotensin I to **angiotensin II**, the active hormone
  - works in several ways to restore fluid volume and BP

Falling BP & Angiotensin II

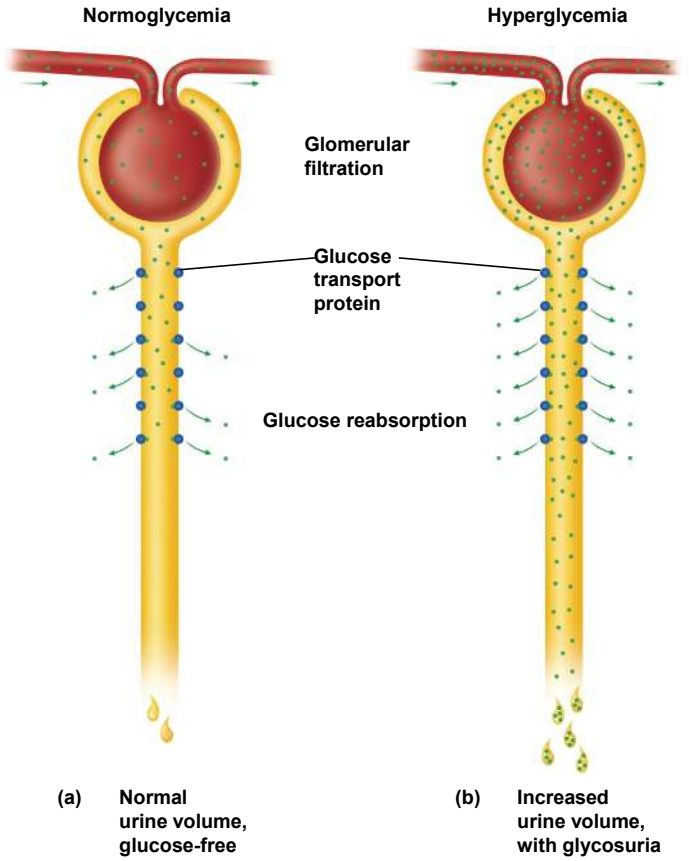


Figure 23.18

- potent vasoconstrictor raising BP throughout body
- constricts efferent arteriole raising GFR despite low BP
- lowers BP in peritubular capillaries enhancing reabsorption of NaCl & H_2O
- angiotensin II stimulates adrenal cortex to secrete aldosterone promoting Na^+ and H_2O reabsorption in DCT and collecting duct
- stimulates posterior pituitary to secrete ADH which promotes water reabsorption by collecting duct
- stimulates thirst & H_2O intake