Human Phys PCB4701

Kidney 1

Kidney Function

Remove waste chemicals, while reabsorbing nutrients

1. Filter plasma from blood (including water & water-soluble nutrients)

2. Reabsorb Na+ : essential to maintain high extracellular [Na+]

3. Reabsorb H_20 : essential to maintain body fluid volume

4. Reabsorb glucose and other nutrients

5. Reabsorb HCO_3 / secrete H+ to maintain pH

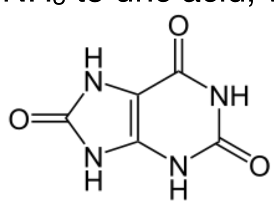
Toxicity of Ammonia (NH_3)

1. NH_3 -> NH_4^+ very basic

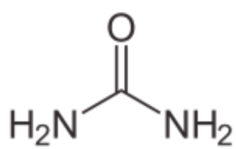
2. NH_3 is metabolic poison

- Fish allow NH_3 to diffuse into surrounding water

- Birds & Reptiles convert NH_3 to uric acid, which is not water soluble and is excreted in the feces.



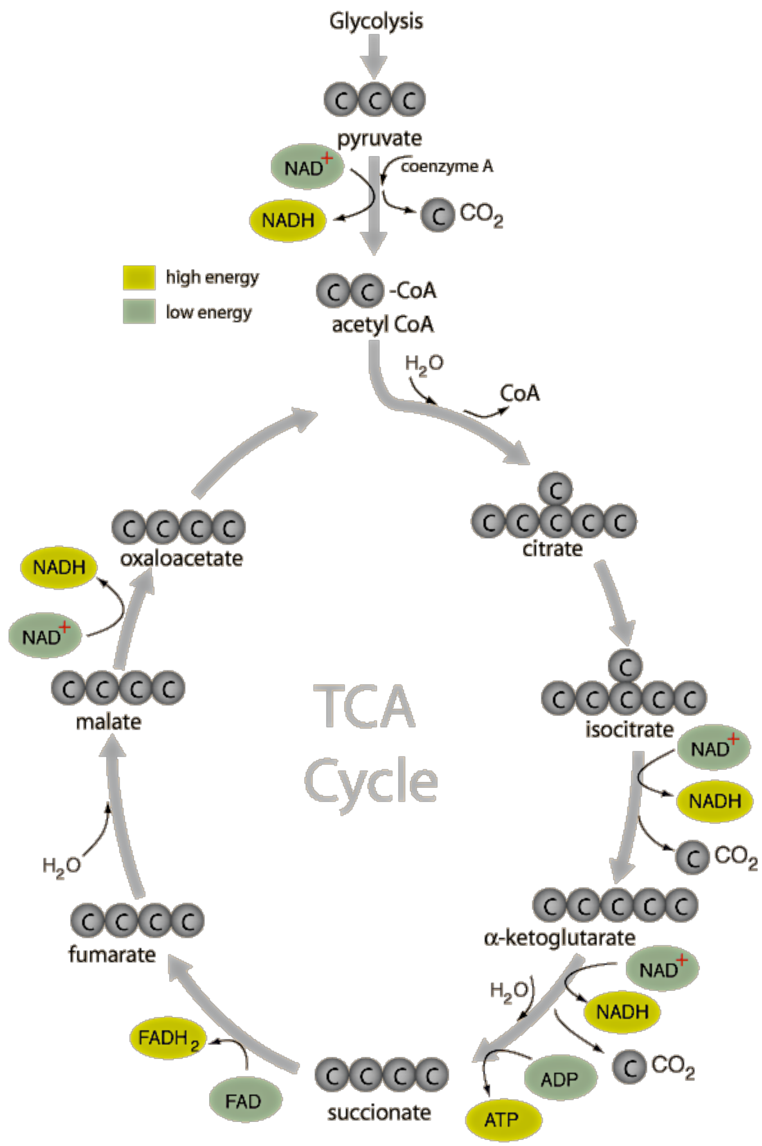
- Mammals convert NH_3 to urea (CH_4N_2O), which is non-toxic and water soluble for excretion by kidney



1828: first organic synthesis: the production of urea without living tissue.

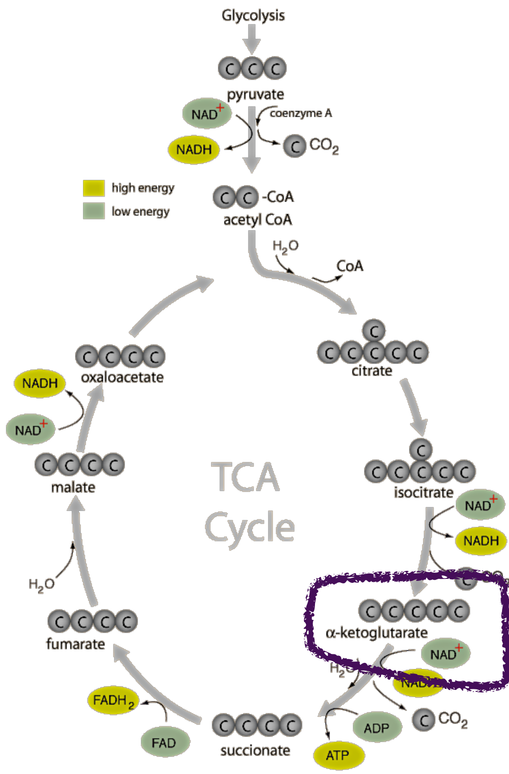
$AgNCO + NH_4Cl \rightarrow (NH_2)_2CO + AgCl$

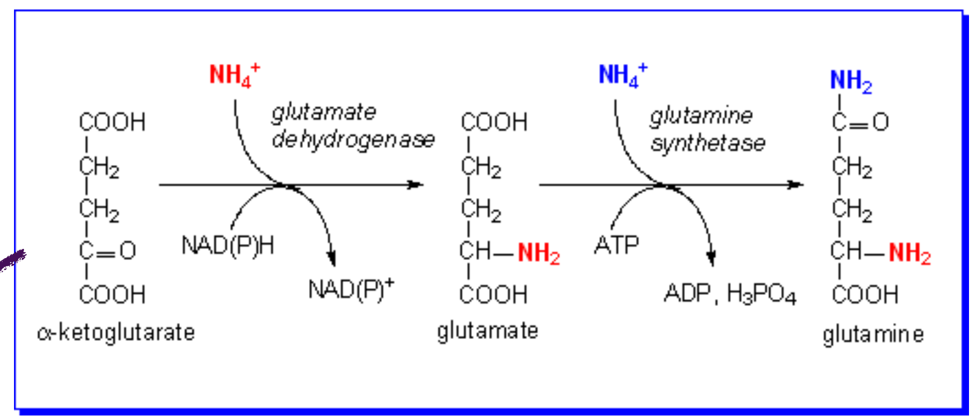
Krebs Cycle



http://hyperphysics.phy-astr.gsu.edu/hbase/biology/tca.html

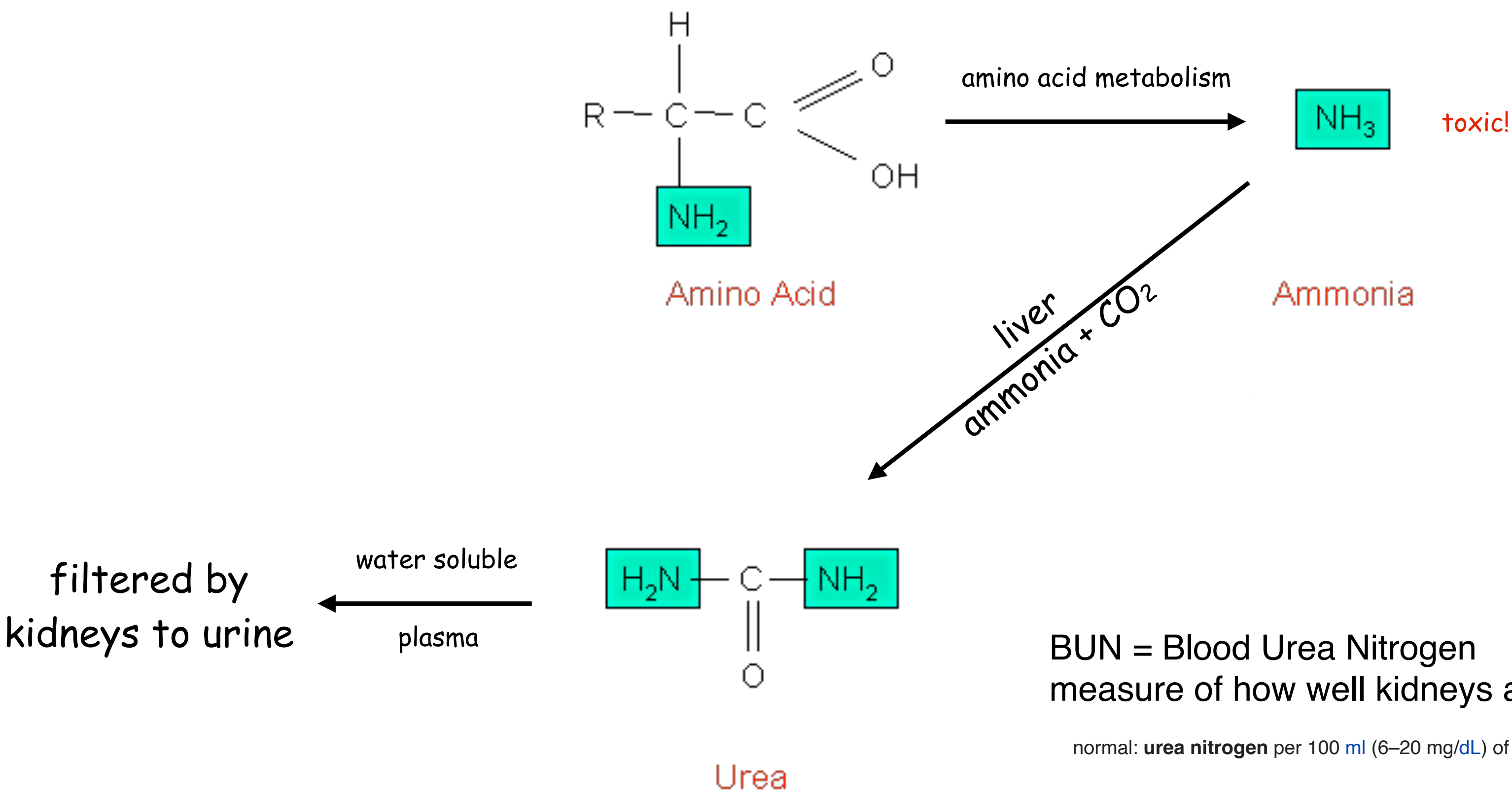
Too much ammonia removes a-ketoglutarate from Krebs cycle, so starves cells of ATP





http://www.ucl.ac.uk/~ucbcdab/urea/amtox.htm

Urea - waste product of excess amino acid metabolism



BUN = Blood Urea Nitrogen
measure of how well kidneys are functioning

normal: **urea nitrogen** per 100 ml (6–20 mg/dL) of blood

Anatomy of the Kidney

Kidney Function
Filter excess and waste chemicals (water soluble) from the blood.
(excess water, Na+, **urea**, glucose > 200 mg/100ml)

Kidney Structures

cortex (bark): reddish brown, lots of capillaries
medulla (inner region): striped with capillaries & collecting ducts;
divided into renal pyramids

urine -> collecting ducts -> minor calyces -> major calyces
-> renal pelvis-> ureters -> urinary bladder -> urethra

calyx; calyces
"cup"

high surface area for exchange, then to storage and outside

ren- Latin for kidney
nephro- Greek for kidney
-uria - problem with urine, e.g. polyuria (too much urine), glycosuria (glucose in urine)
diabetes - also means too much urine

Figure 17.1

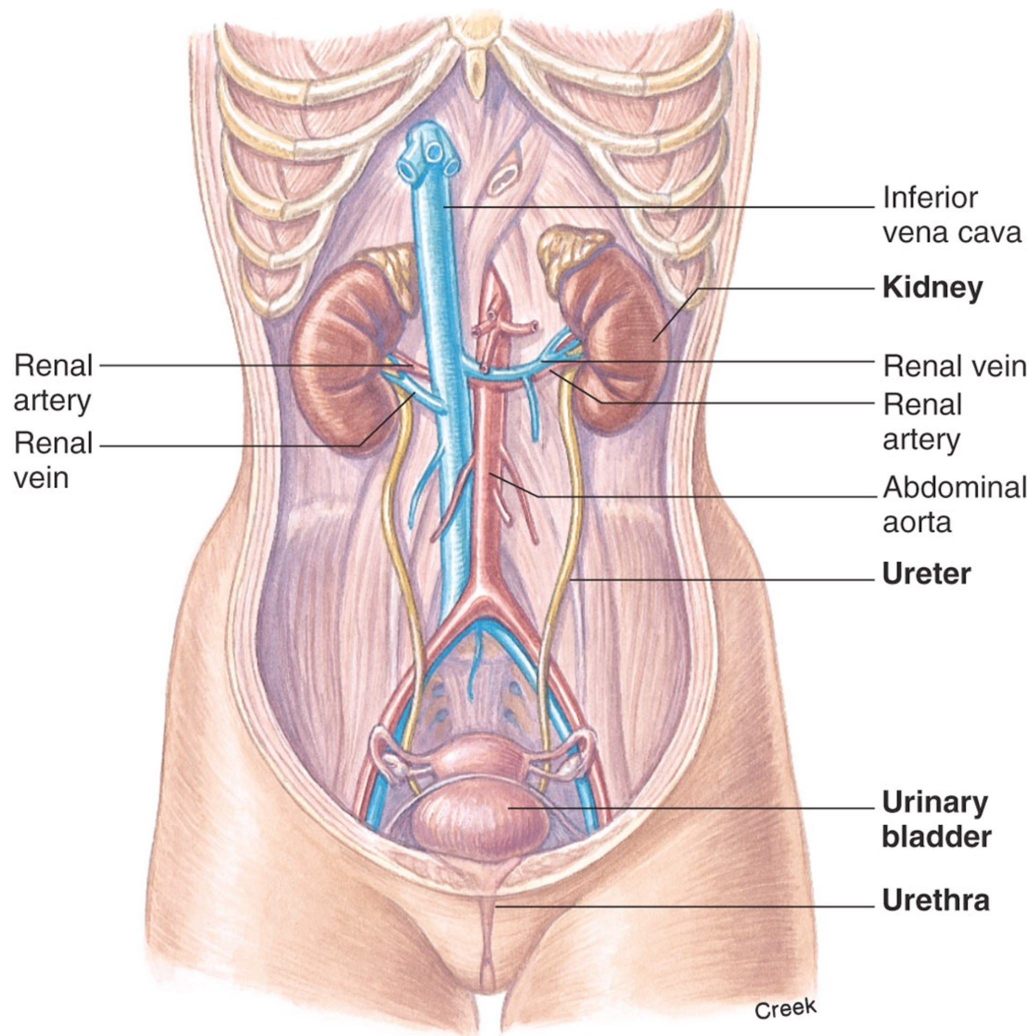
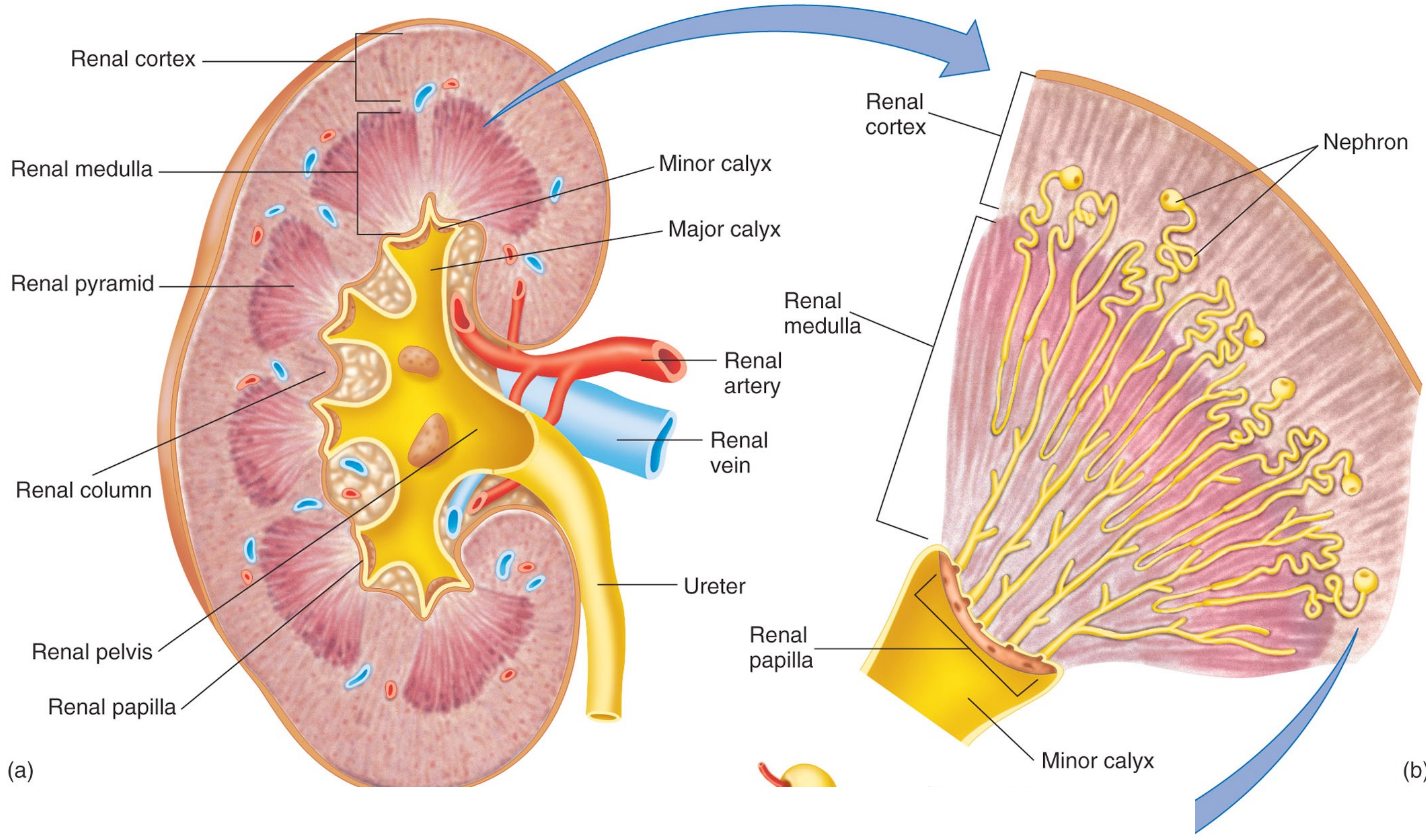
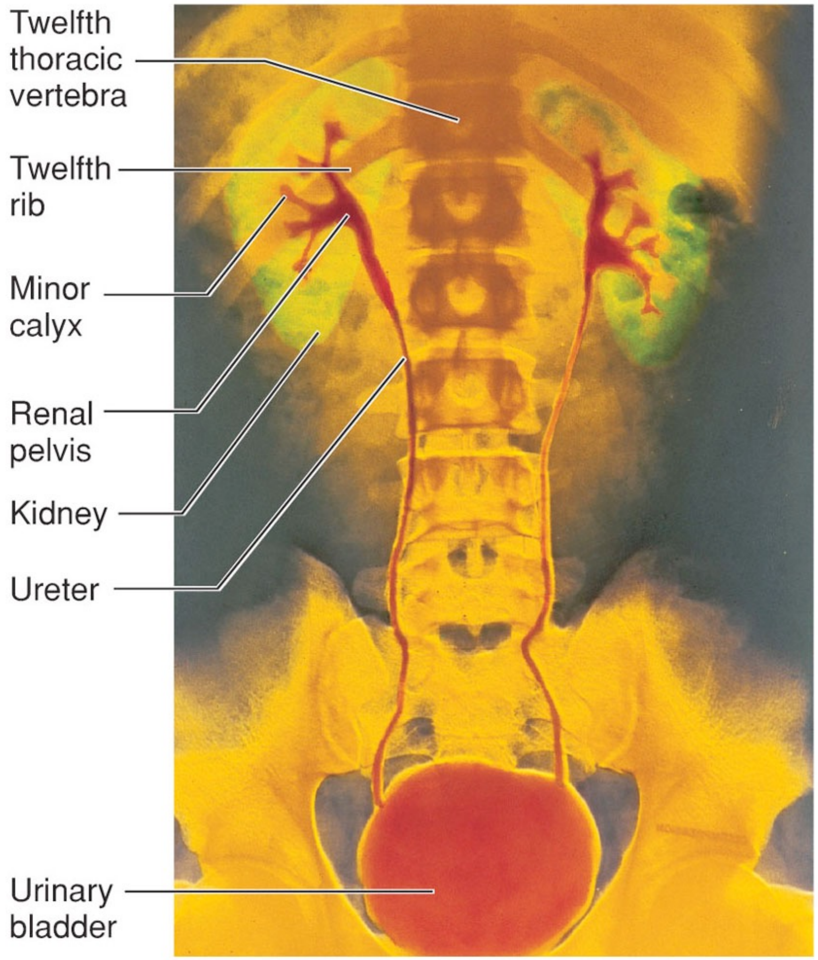

Inferior vena cava
Kidney
Renal artery
Renal vein
Renal vein
Renal artery
Abdominal aorta
Ureter
Urinary bladder
Urethra
Creek

Figure 17.2



Renal cortex
Renal medulla
Renal pyramid
Renal column
Renal pelvis
Renal papilla
Minor calyx
Major calyx
Renal artery
Renal vein
Ureter
(a)
Renal cortex
Renal medulla
Nephron
Renal papilla
Minor calyx
(b)

Figure 17.3


Twelfth thoracic vertebra
Twelfth rib
Minor calyx
Renal pelvis
Kidney
Ureter
Urinary bladder

ren- Latin for kidney
nephro- Greek for kidney

Nephron
functional unit of the kidney: filters small molecules from blood, reabsorbs and secretes chemicals to produce urine.

glomerular (Bowman's) capsule - filters blood in cortex

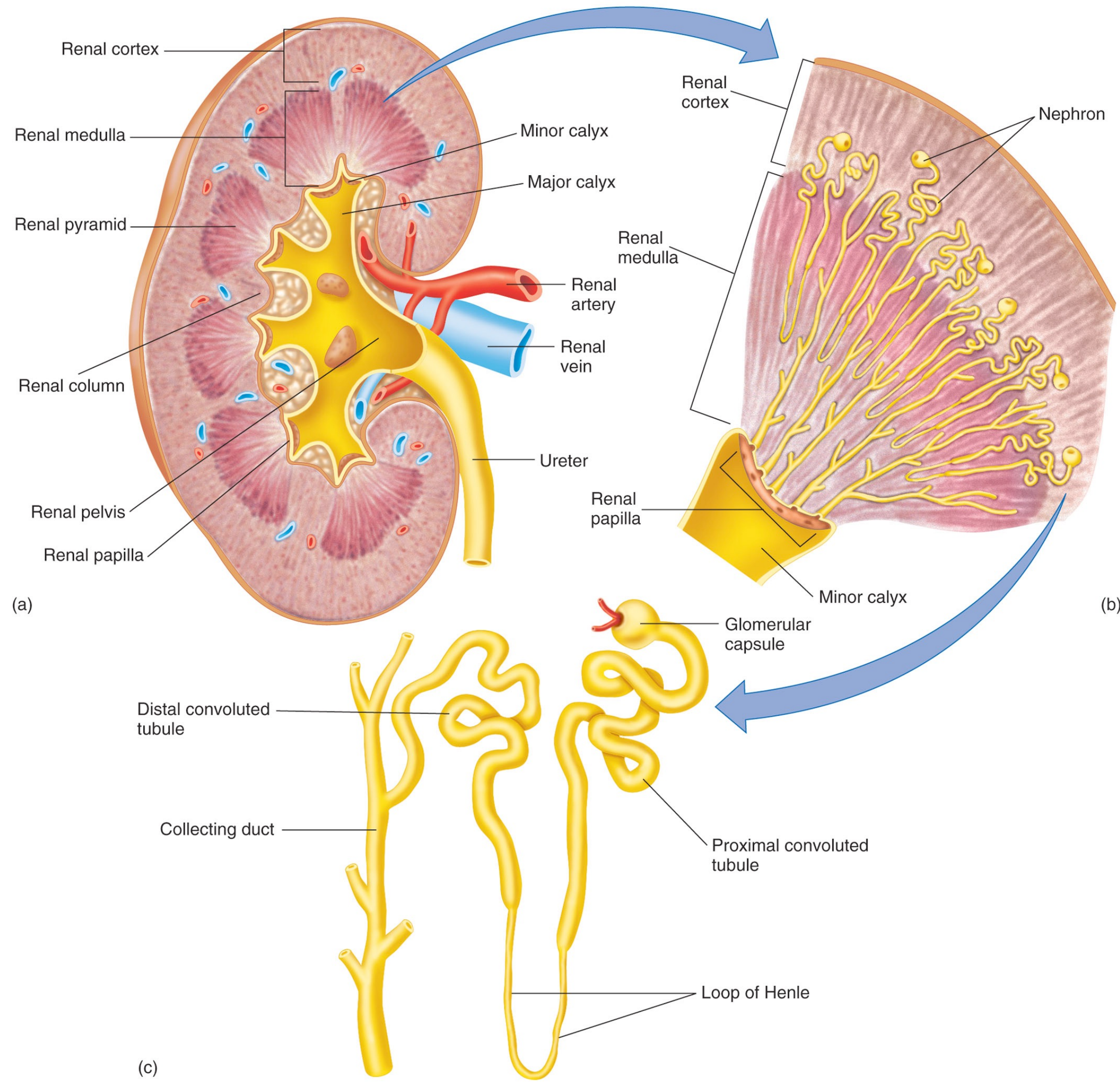
proximal convoluted tubule (closer to glomerulus) starts in cortex

loop of Henle dives into medulla

distal convoluted tubule (further from glomerulus) back to cortex

collecting duct final fluid **(**urine) drains into calyces & pelvis

Figure 17.2


Renal cortex
Renal medulla
Renal pyramid
Renal column
Renal pelvis
Renal papilla
Minor calyx
Major calyx
Renal artery
Renal vein
Ureter
(a)
Renal cortex
Nephron
Renal medulla
Renal papilla
Minor calyx
(b)
Glomerular capsule
Distal convoluted tubule
Collecting duct
Proximal convoluted tubule
Loop of Henle
(c)

Kidney Vasculature (blood supply)

renal artery -> interlobar arteries -> arcuate arteries -> interlobular arteries -> arterioles

-> glomeruli -> peritubular capillaries -> ← capillary beds for exchange & transport

interlobular veins -> arcuate veins -> interlobar veins -> renal vein

Figure 17.4

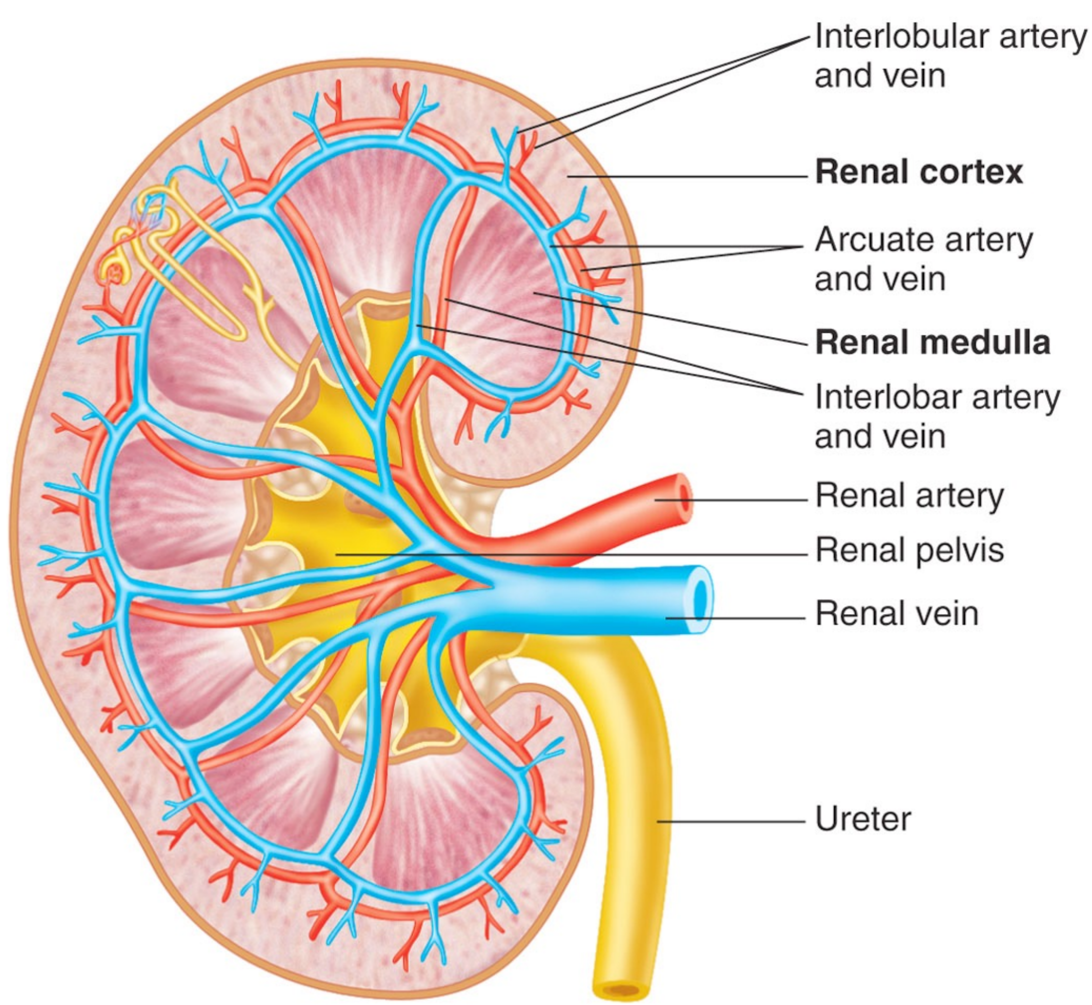
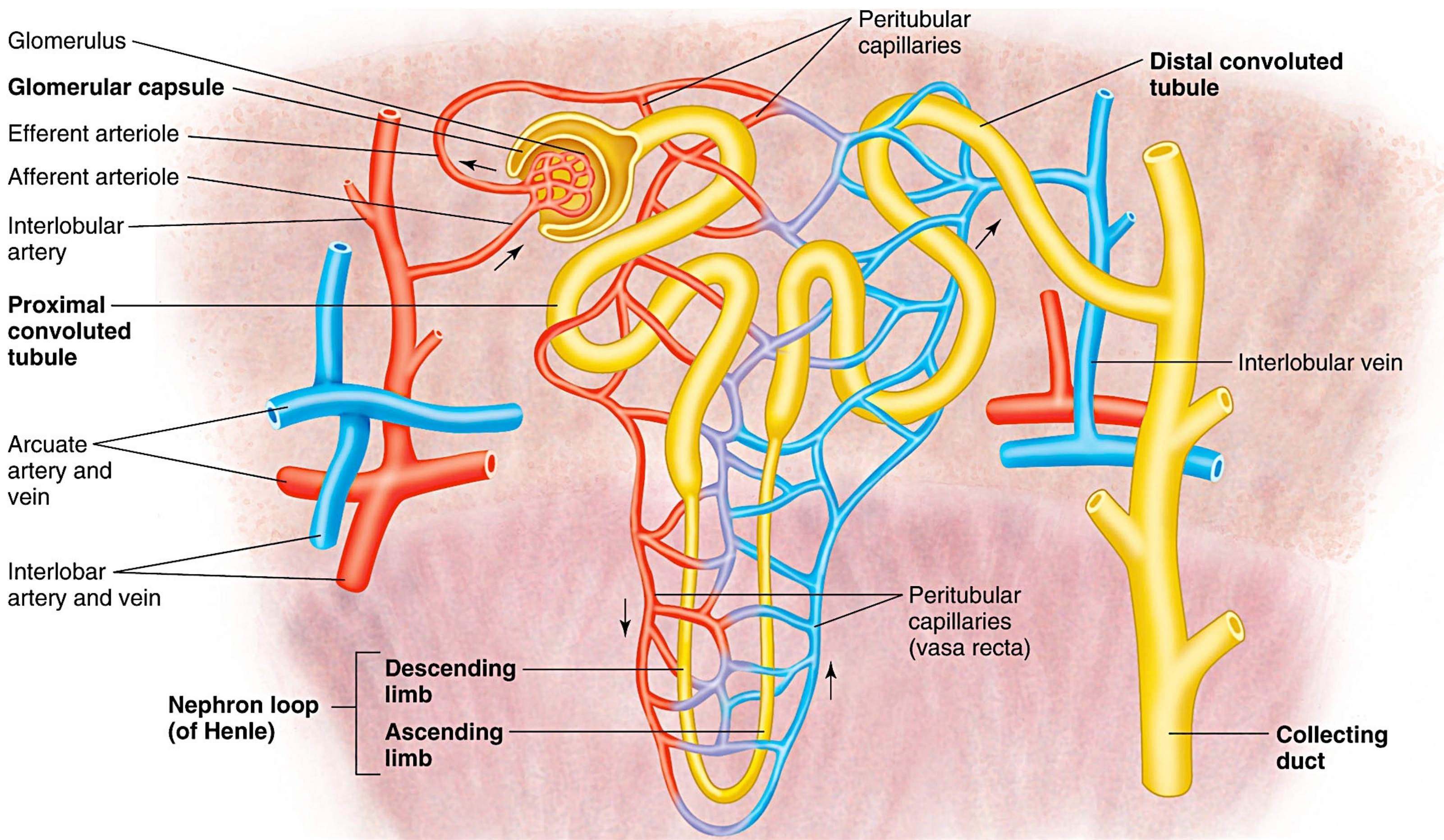

Interlobular artery and vein
Renal cortex
Arcuate artery and vein
Renal medulla
Interlobar artery and vein
Renal artery
Renal pelvis
Renal vein
Ureter

Figure 17.5



Glomerulus
Glomerular capsule
Efferent arteriole
Afferent arteriole
Interlobular artery
Proximal convoluted tubule
Arcuate artery and vein
Interlobar artery and vein
Peritubular capillaries
Distal convoluted tubule
Interlobular vein
Peritubular capillaries (vasa recta)
Nephron loop (of Henle)
Descending limb
Ascending limb
Collecting duct

2 capillary beds in Renal Circulation

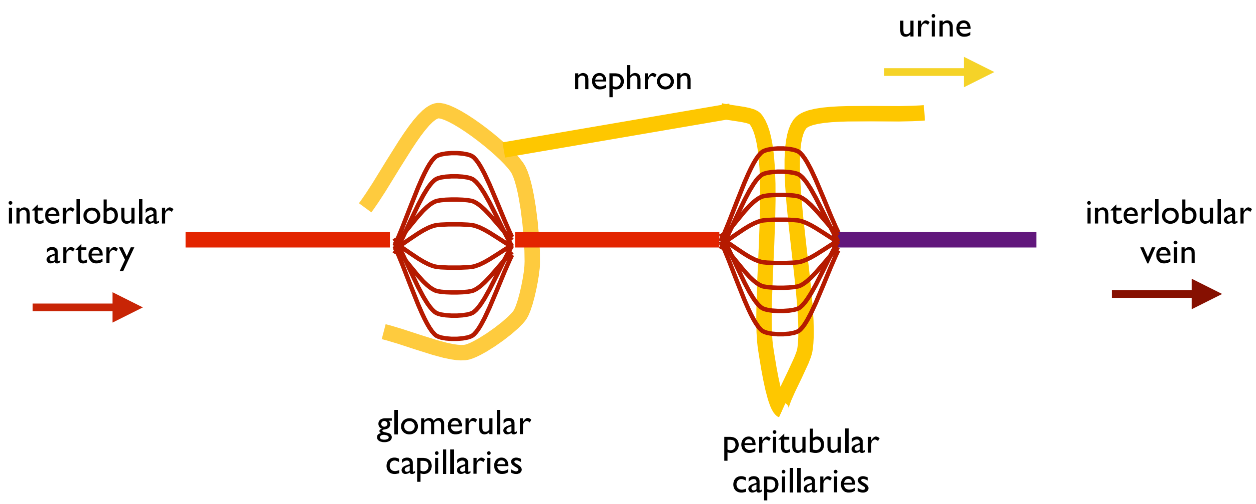
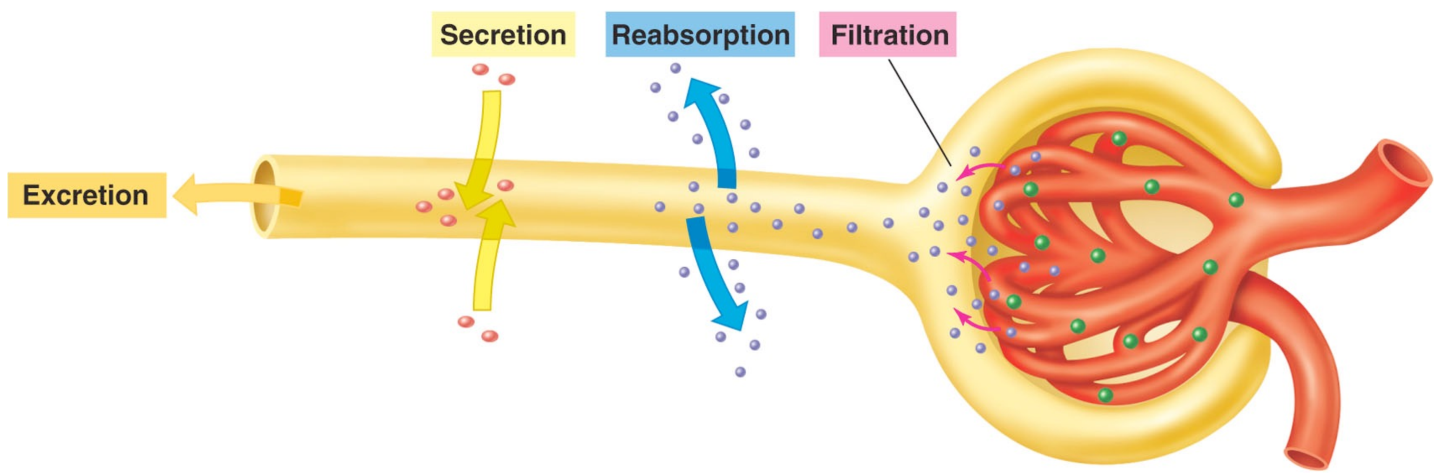


Figure 17.21

1. Filter plasma and water soluble chemicals **from** blood into urine

2. Reabsorb and return needed chemicals from urine and back to blood

3. Secrete additional chemicals into the urine



Glomerular Filtration

Plasma is filtered. Under blood pressure, fluid moves from capillaries to glomerular lumen as **filtrate**.

3 Layers of Filtration:

Fenestra of glomerular capillaries allows plasma but not platelets, blood cells to enter filtrate.

Basement Membrane layer of collagen and proetoglycans restricts flow into glomerular lumen.

Slit Diaphragm of the inner layer of glomerular capsule made of **podocytes**, which have interdigitated **pedicels** (foot processes) that wrap around glomerular capillaries. Blocks proteins from entering filtrate.

Net pressure for filtration =
hydrostatic pressure of blood (pushing fluid out of capillaries)
– osmotic pressure of proteins (pulling fluid back into capillaries)
= 10 mmHg

Glomerular Capsule filters small molecules (not proteins) from blood into nephron.

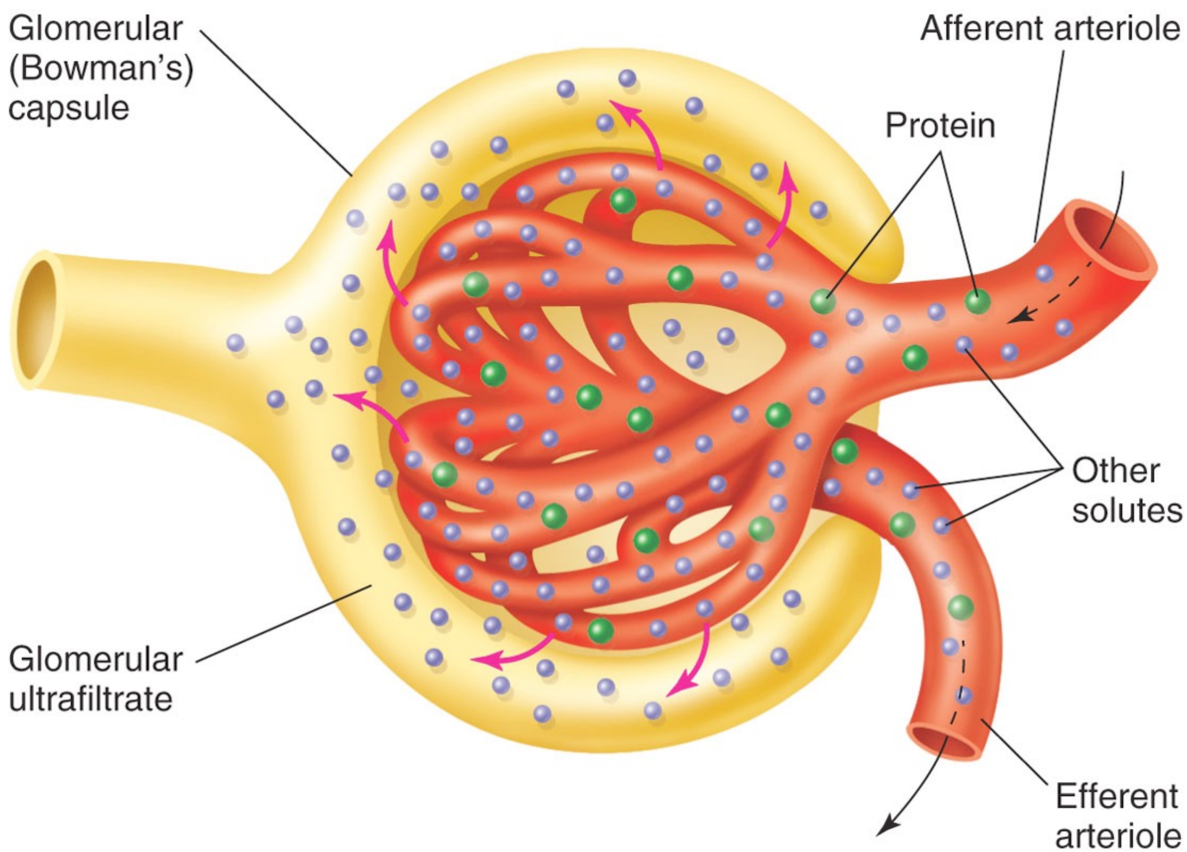


Figure 17.10

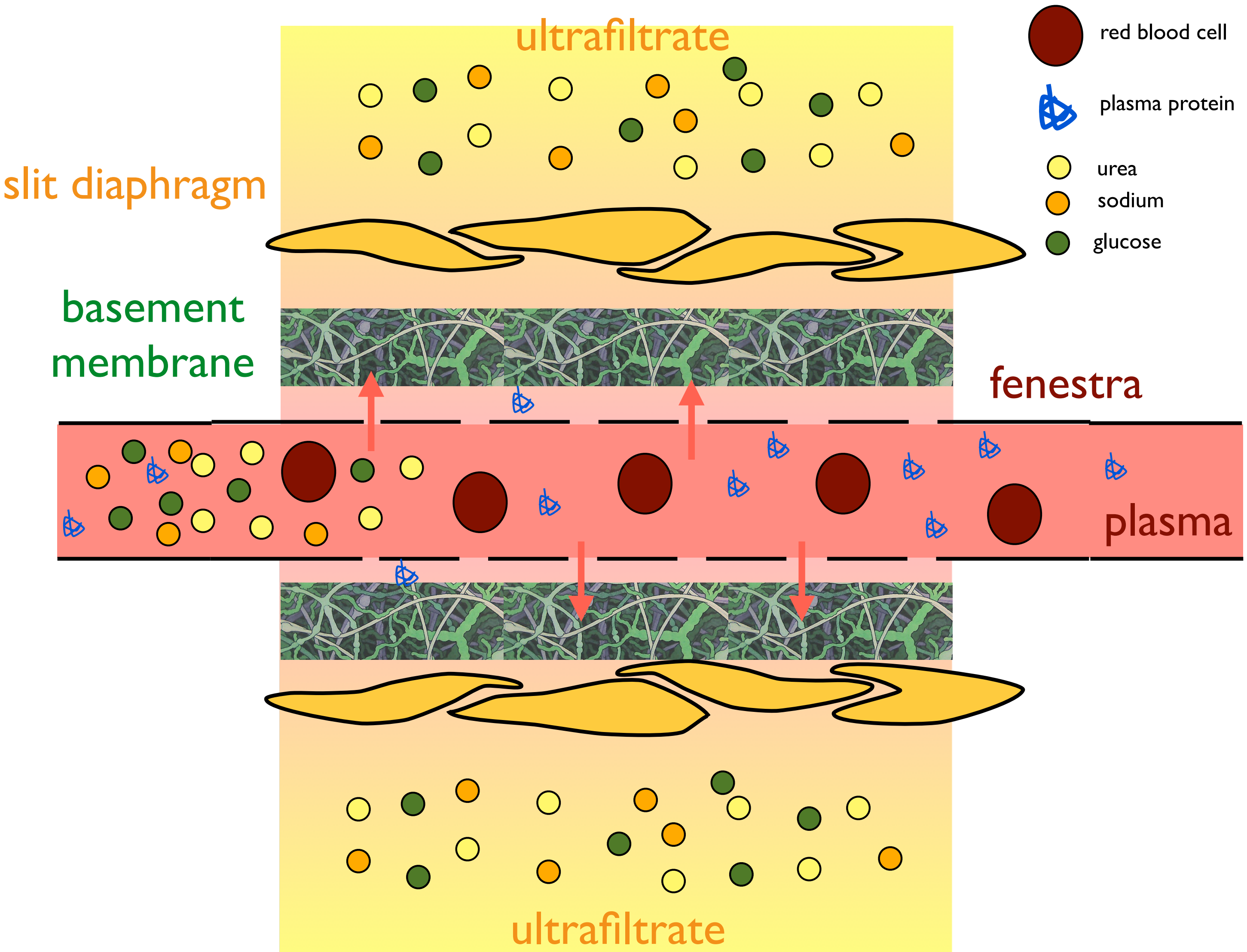
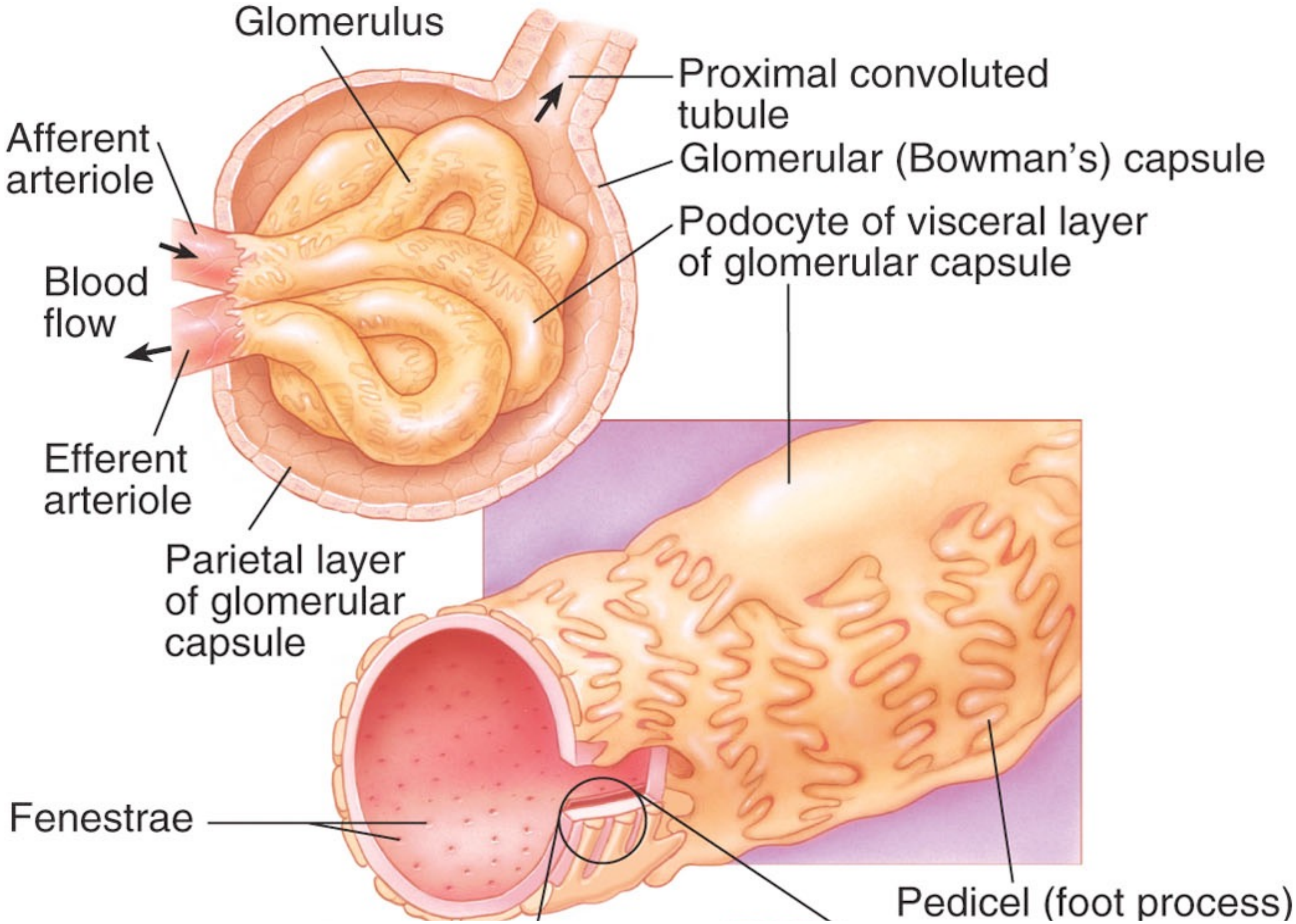

ultrafiltrate
slit diaphragm
basement
membrane
fenestra
plasma
ultrafiltrate
red blood cell
plasma protein
urea
sodium
glucose

Figure 17.8



Glomerulus
Proximal convoluted tubule
Glomerular (Bowman's) capsule
Afferent arteriole
Podocyte of visceral layer of glomerular capsule
Blood flow
Efferent arteriole
Parietal layer of glomerular capsule
Fenestrae
Pedicel (foot process)

Figure 17.8

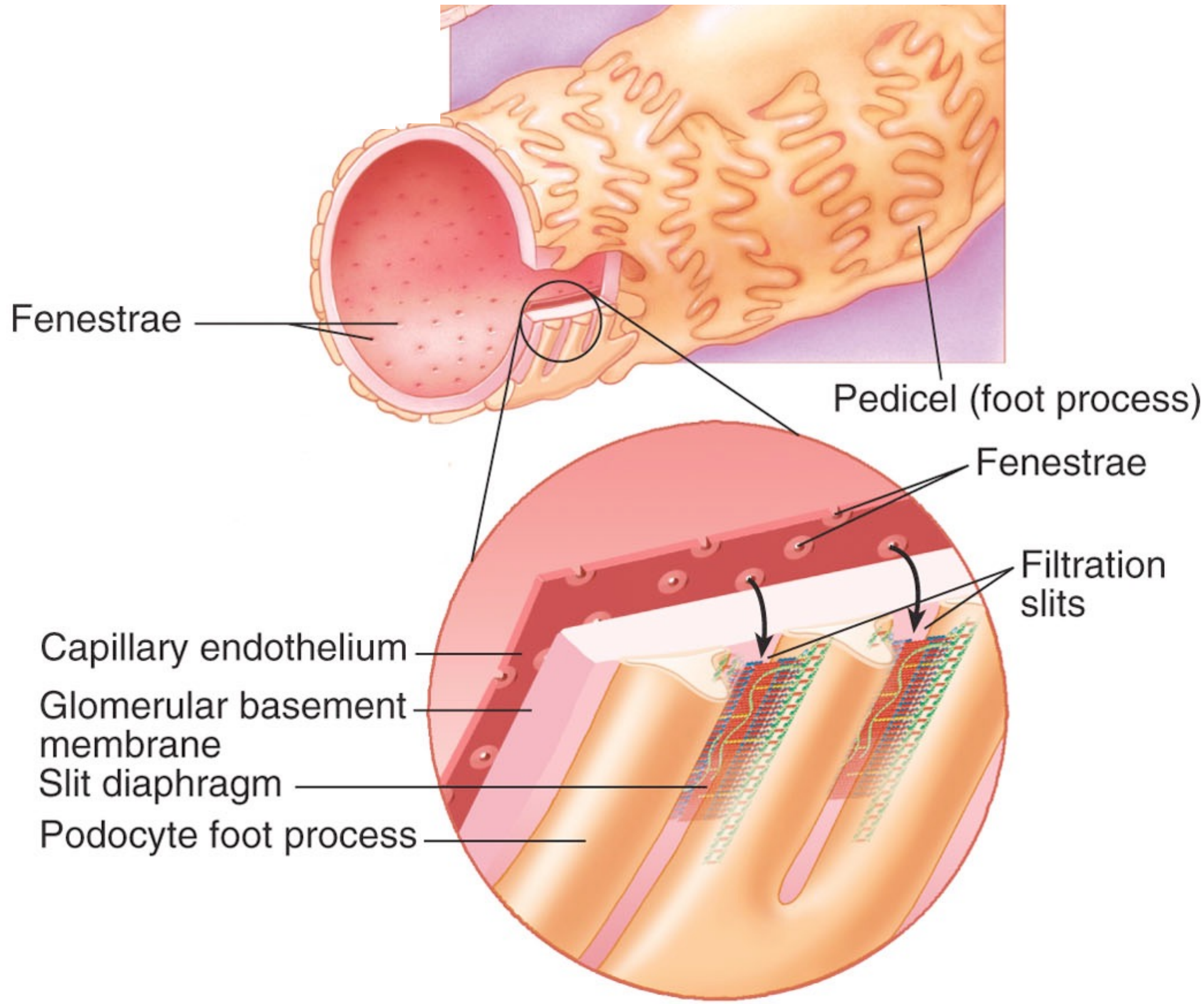
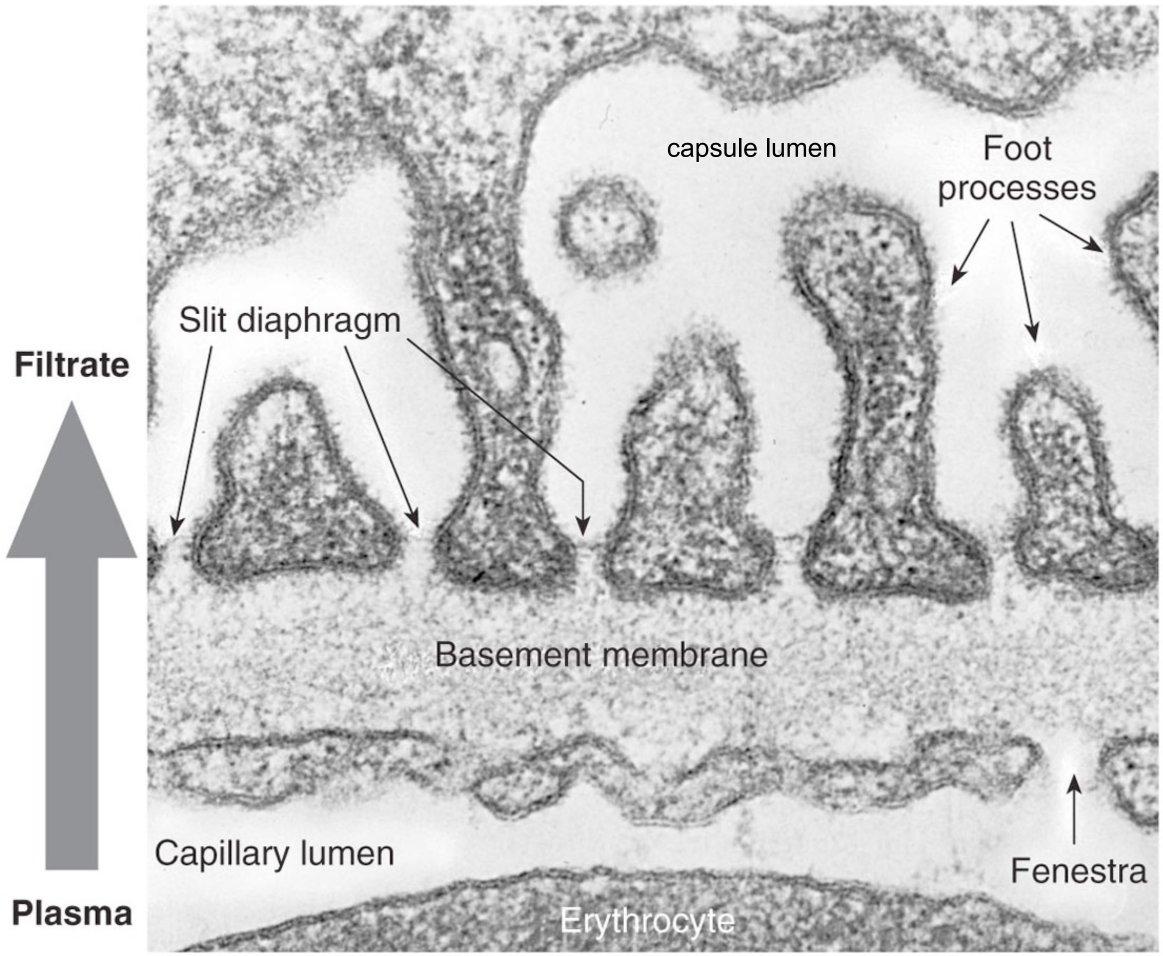

Fenestrae
Pedicel (foot process)
Fenestrae
Filtration slits
Capillary endothelium
Glomerular basement membrane
Slit diaphragm
Podocyte foot process

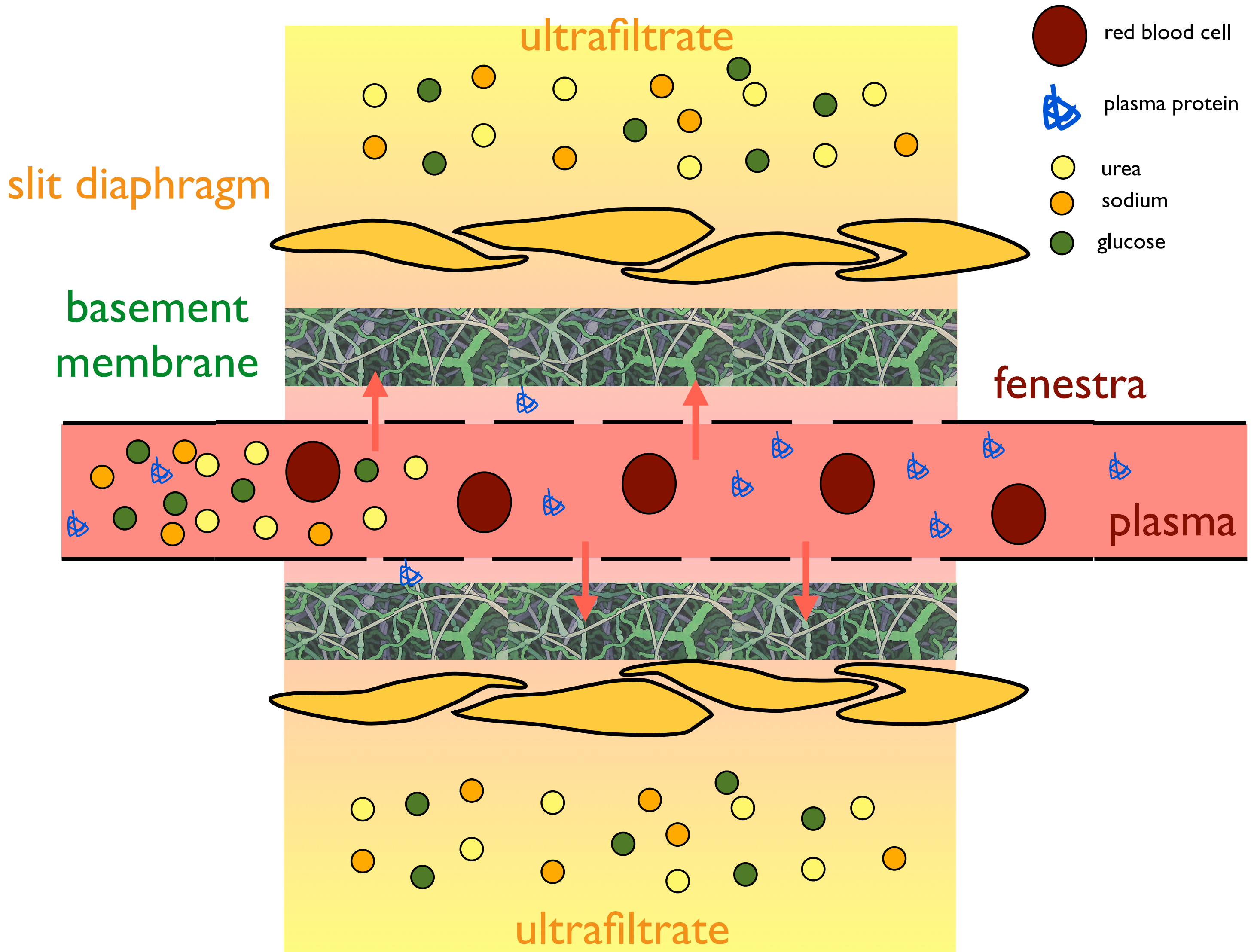
Figure 17.7


Podocyte cell body
Primary process of podocyte
Branching pedicels

Figure 17.9



capsule lumen
Foot
processes
Slit diaphragm
Filtrate
Basement membrane
Capillary lumen
Fenestra
Plasma
Erythrocyte


ultrafiltrate
red blood cell
plasma protein
urea
sodium
glucose
slit diaphragm
basement
membrane
fenestra
plasma
ultrafiltrate

Glomerular Capsule filters small molecules (not proteins) from blood into nephron.

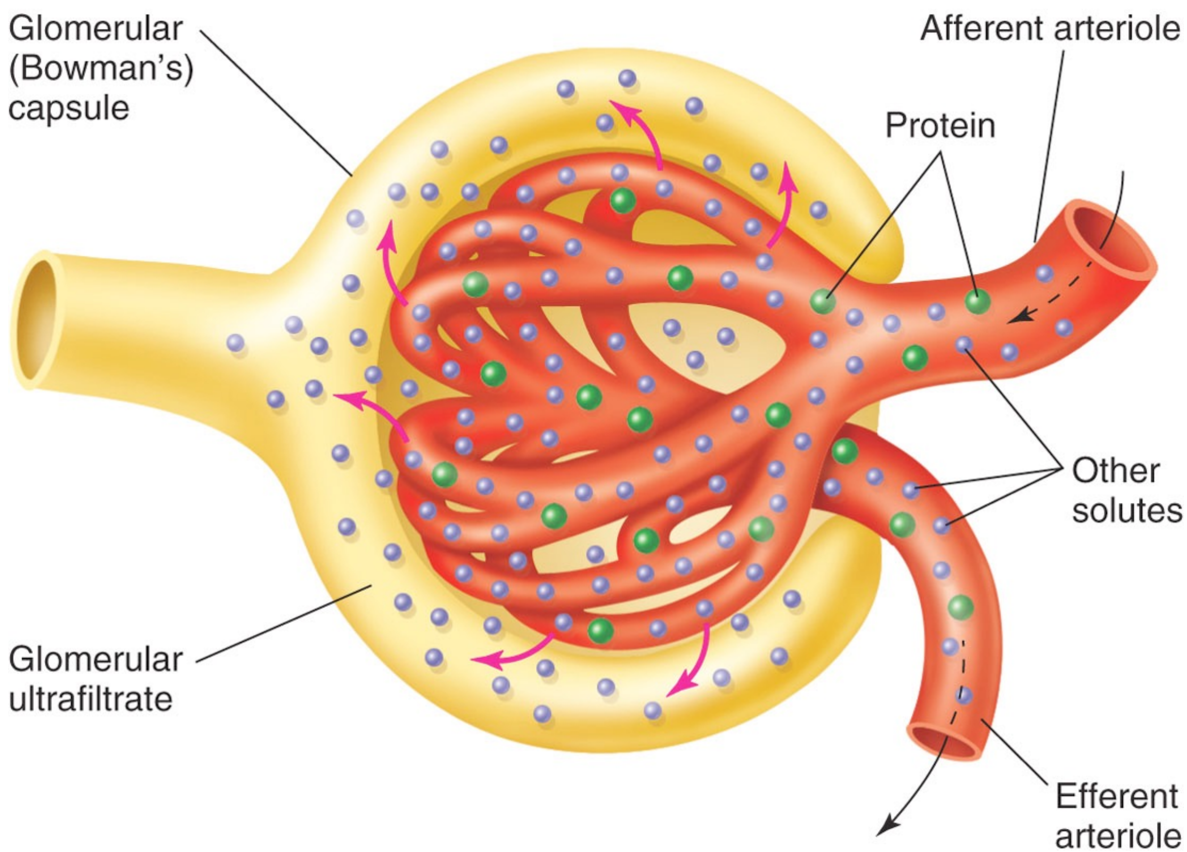


Figure 17.10

Glomerular Filtration Rate (GFR)

GFR = volume of filtrate produced by both kidneys each minute

= 120 ml / minute

= 180 L per day

Blood volume = 5-6 L, so total blood volume filtered every 40 minutes.

Urine volume = 1-2 L /day.

Therefore, most of water in filtrate must be reabsorbed.

plasma creatinine (muscle waste product) eliminated by glomerular filtration;
kidney disease -> low GFR -> high plasma creatinine levels

Regulation of GFR

sympathetic nervous system (norepi)

-> vasoconstriction of kidney arterioles

-> decreased GFR

Renal Autoregulation also keeps GFR constant

decreased blood pressure -> dilation of kidney arterioles

increased blood pressure -> constriction of kidney arterioles

(caused by smooth muscle of arterioles and chemicals produced by nephron)

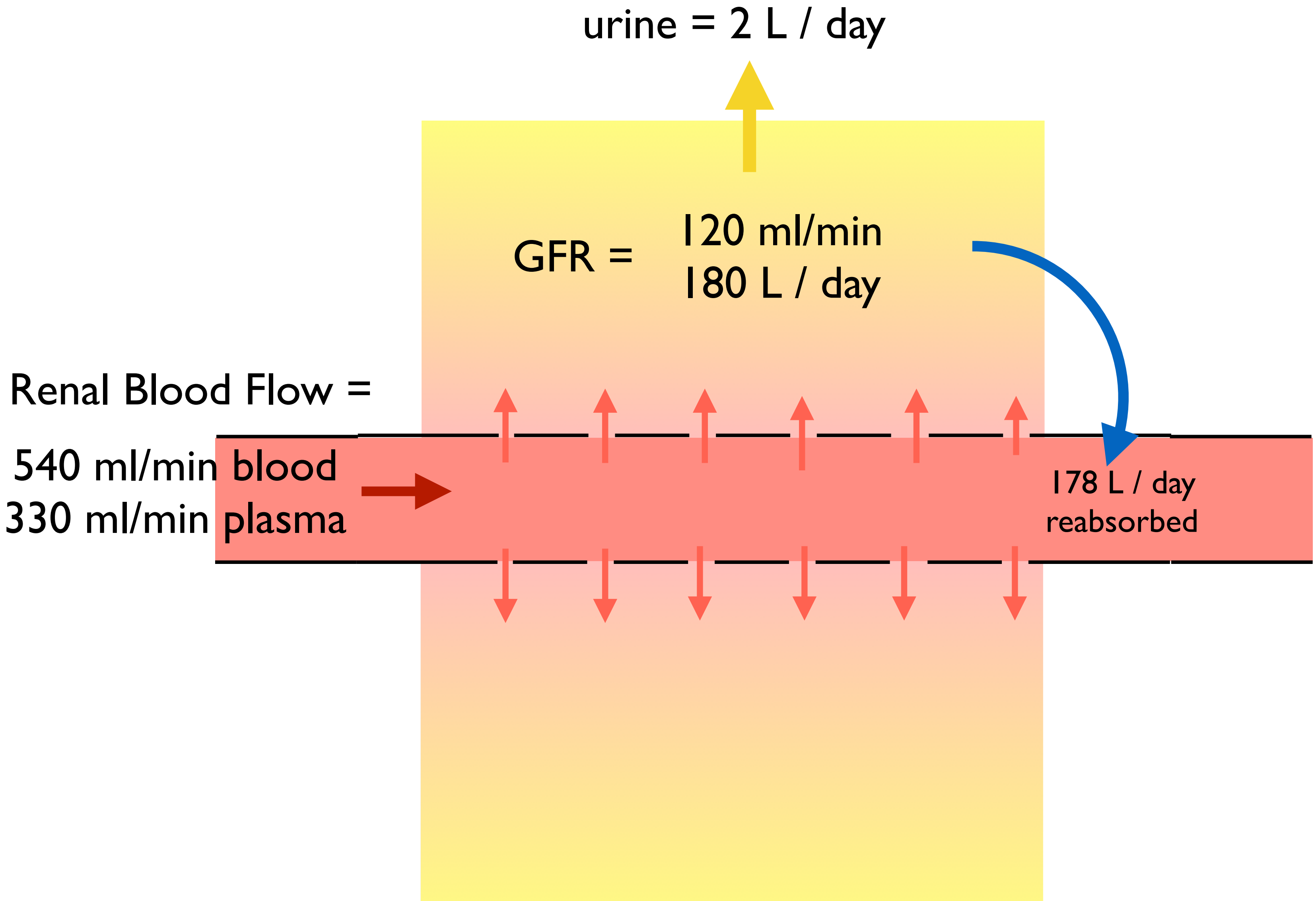

urine = 2 L / day
GFR =
120 ml/min
180 L / day
Renal Blood Flow =
540 ml/min blood
330 ml/min plasma
178 L / day
reabsorbed

Table 17.1

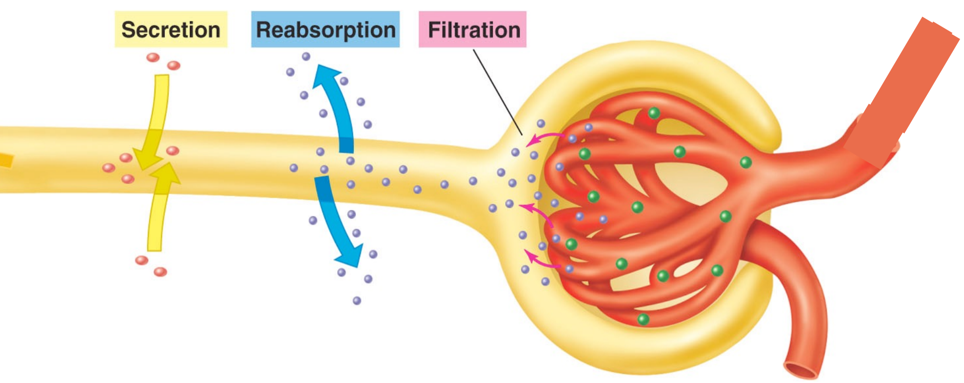
Table 17.1 | Regulation of the Glomerular Filtration Rate (GFR)

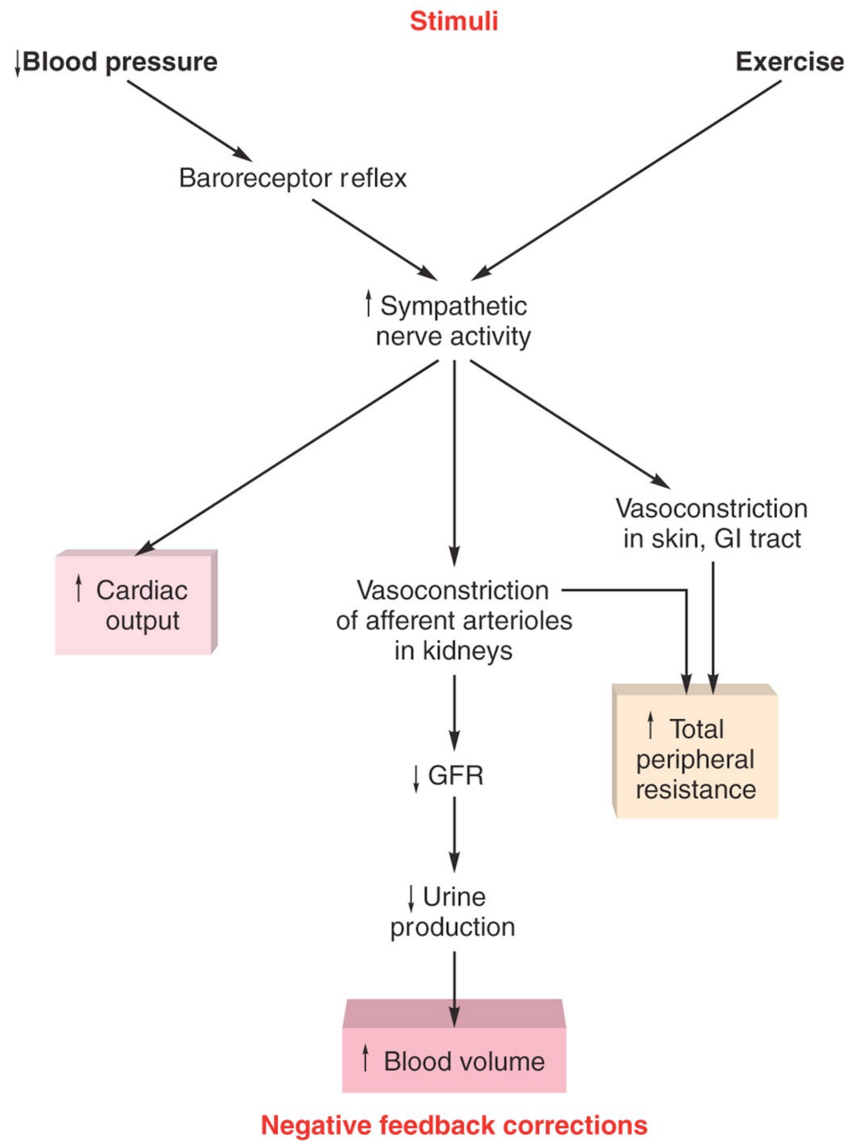
Regulation	Stimulus	Afferent Arteriole	GFR
Sympathetic nerves	Activation by baroreceptor reflex or by higher brain centers	Constricts	Decreases
Autoregulation	Decreased blood pressure	Dilates	No change
Autoregulation	Increased blood pressure	Constricts	No change

Figure 17.11

Vasoconstriction of arterioles

→⬇GFR





Reabsorption of Filtrate

GFR = 180 L/day

Filtrate is isotonic with plasma (i.e 0.15M NaCl)

minimum urine production = 400 ml/day
(**obligatory water loss** required to get rid of metabolic waste chemicals)

Must reabsorb up to 99% + of filtrate.

Three steps to reabsorption:

1. Reabsorption of NaCl and Water from proximal tubule

2. Reabsorption of NaCl and Water by Countercurrent Multiplier of loop of Henle

3. Reabsorption of Water through aquaporin channels in the collecting ducts

Reabsorption of Salt and Water

85% of filtered water and NaCl is reabsorbed in **proximal tubule**.

Epithelial cells pump Na+ into interstitial fluid with Na+/K+ ATPase, which creates a concentration gradient for Na+ (and an electrical gradient).

Na+ diffuses from tubule -> epithelial cell -> pumped into interstitial fluid
Cl- follows positive charge of Na+ by passive diffusion
Water follows NaCl into interstitial fluid by osmosis

Requires energy (6% of total calories)

Remaining 15% of fluid reabsorbed by ascending limb of loop of Henle and collecting duct, depending on hydration state.

Figure 17.5

85% of filtered water and NaCl is reabsorbed in

proximal tubule.

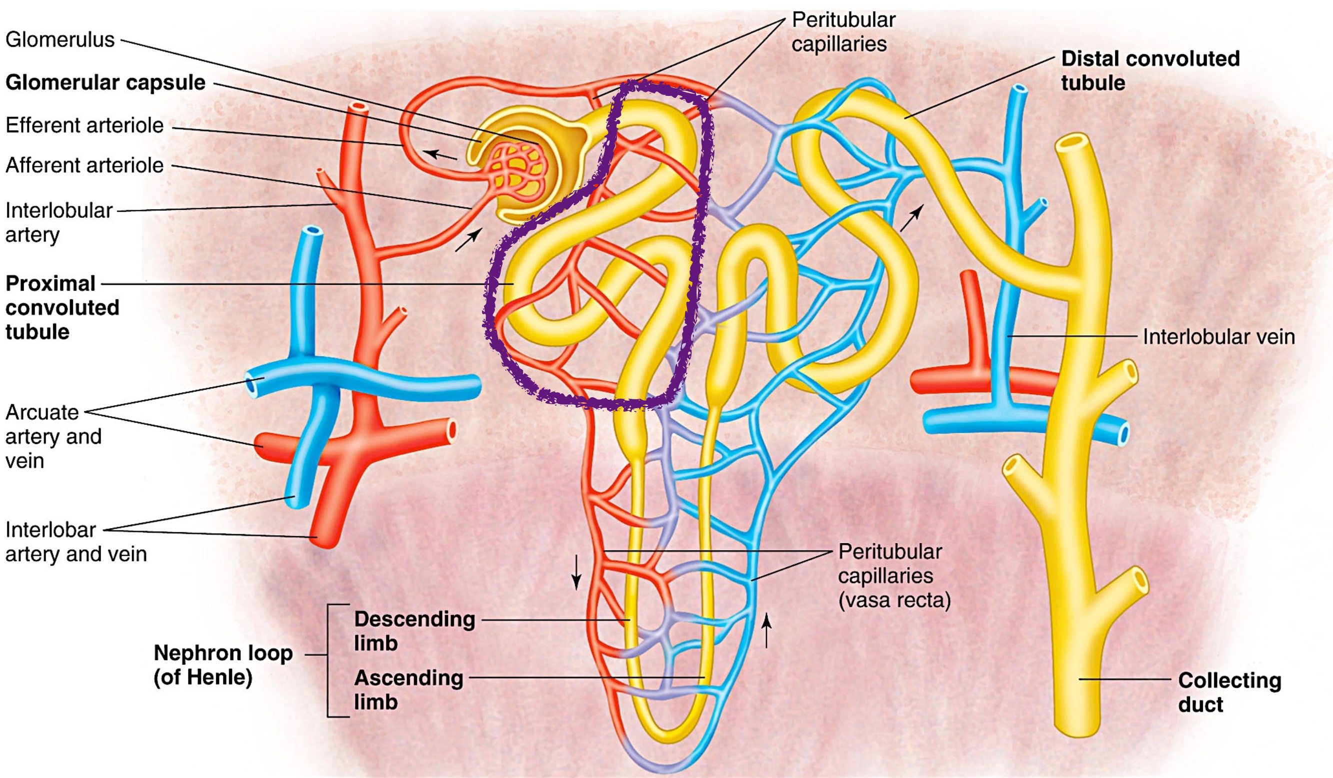
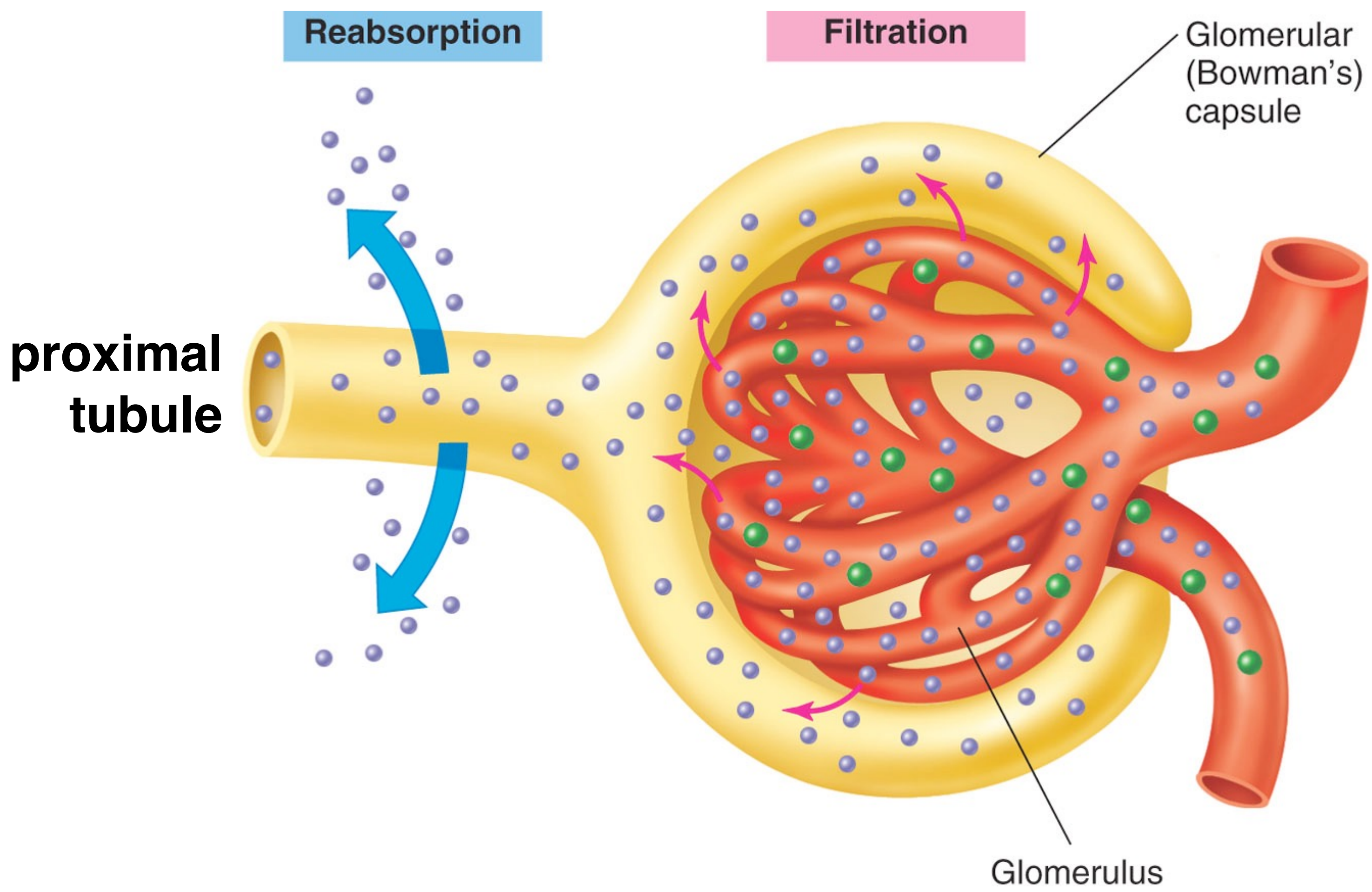


Figure 17.12



Reabsorption
Filtration
Glomerular (Bowman's) capsule
proximal tubule
Glomerulus

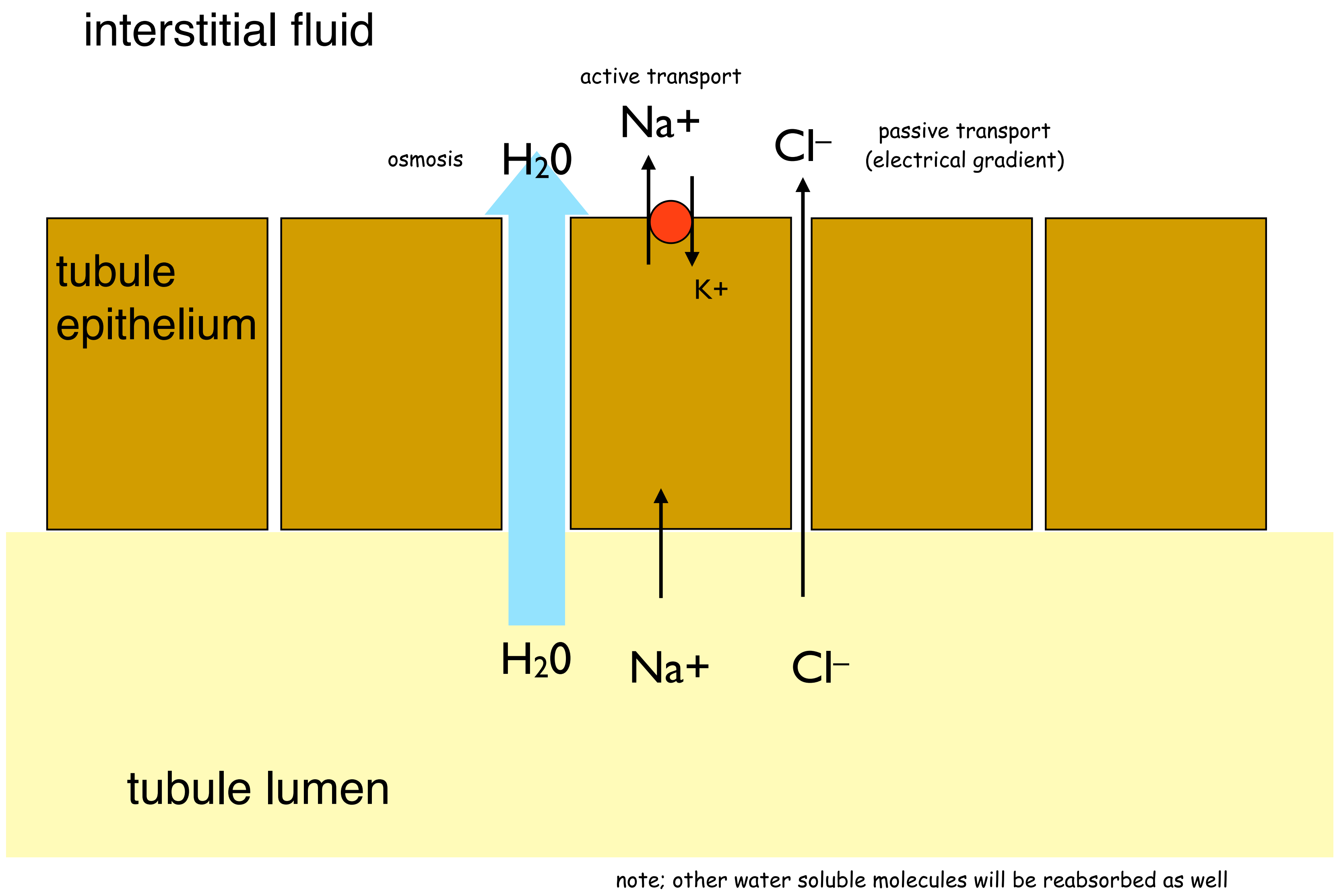
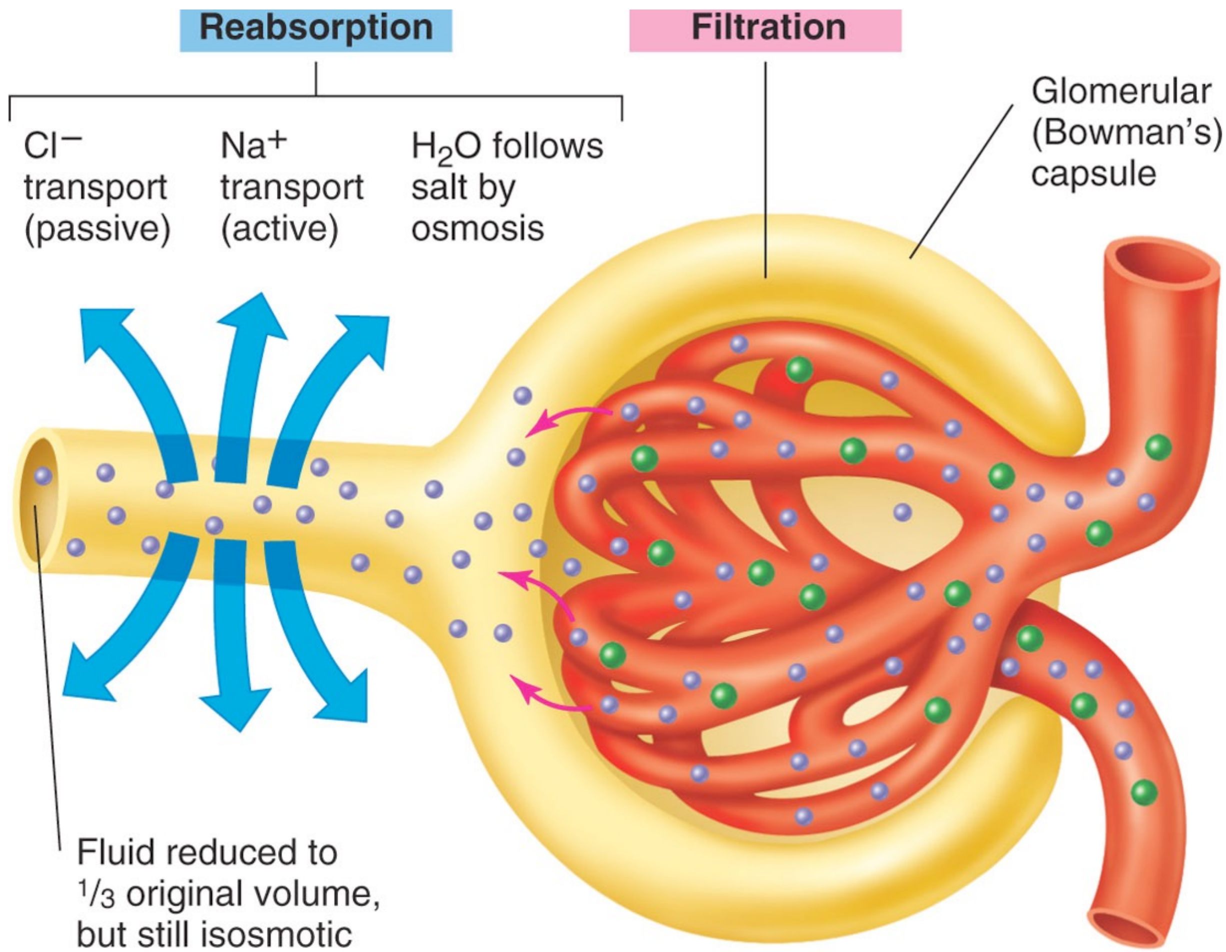

interstitial fluid
active transport
Na+
osmosis
H20
Cl–
passive transport
(electrical gradient)
tubule
epithelium
K+
H20
Na+
Cl–
tubule lumen
note; other water soluble molecules will be reabsorbed as well

Figure 17.13



Reabsorption
Filtration
Cl^- transport (passive)
Na^+ transport (active)
H_2O follows salt by osmosis
Glomerular (Bowman's) capsule
Fluid reduced to 1/3 original volume, but still isosmotic

Reabsorption of Glucose

Glucose transporters in the **proximal tubule** reabsorb glucose by Na+/glucose co-transport into epithelial cells, and then diffusion into blood.

Transporters require Na+ gradient (set up by Na+/K+ ATPase pumps).

Transporters are **saturable**: maximum transport (T_m) is 375 mg/minute glucose.

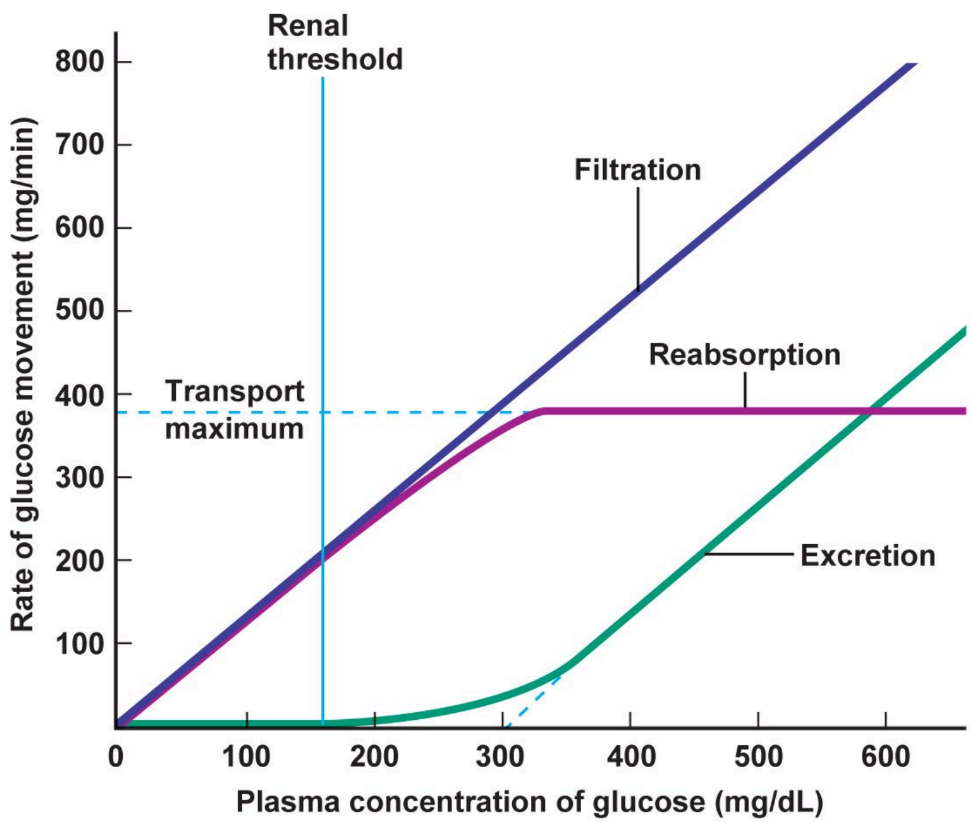
Fasting glucose = 1 mg/ml (= 100 mg/100ml).
GFR = 125 ml/min
so glucose filtration = 125 mg/min (which is less than T_m of 375 mg/min)
so normally no glucose in urine

Renal Plasma Threshold is maximum concentration that can still be excreted into urine.

Renal plasma threshold for glucose = 200 mg/100 ml; above 200 mg/100ml, glucose appears in urine (**glycosuria**)

(similar mechanism of amino acid reabsorption)

When Renal Plasma Threshold of plasma glucose is exceeded, then proximal tubule cannot reabsorb all the filtered glucose: excess -> urine (glycosuria)



Na+/glucose co-transport

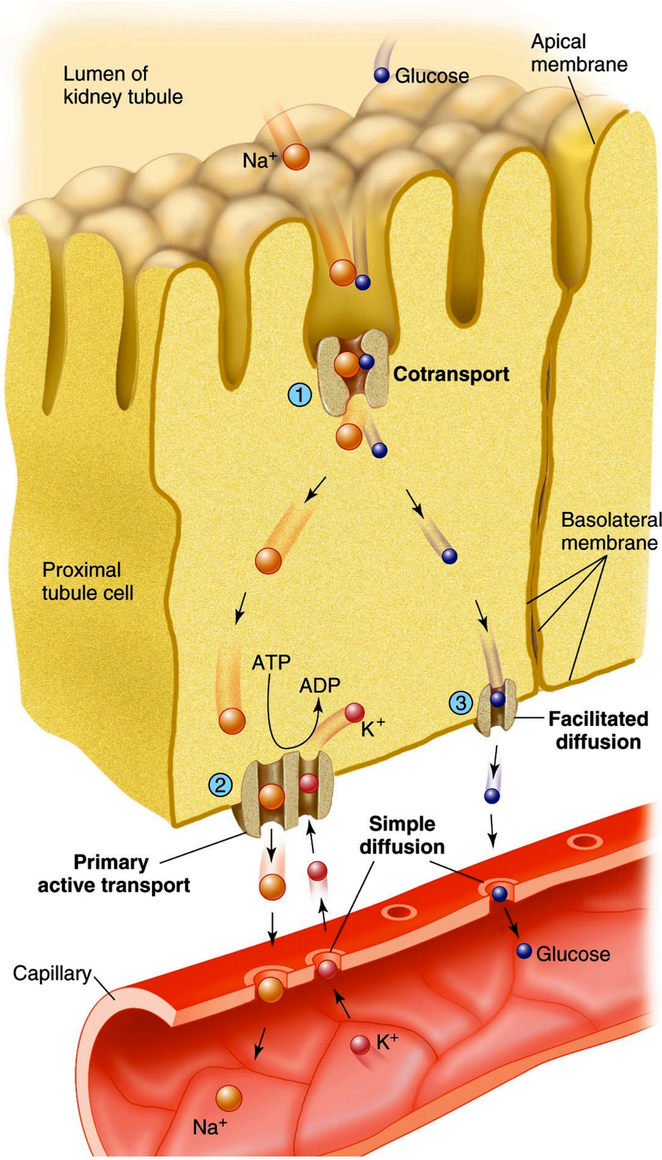


Figure 17.24

Reabsorption of Bicarbonate: Acid-Base Balance

Urine slightly **acidic** (pH 5 - 7)

Na+/H+ exchanger in proximal tubule moves H+ into urine (relies on Na+ gradient set up by Na+/K+ ATPase pump)

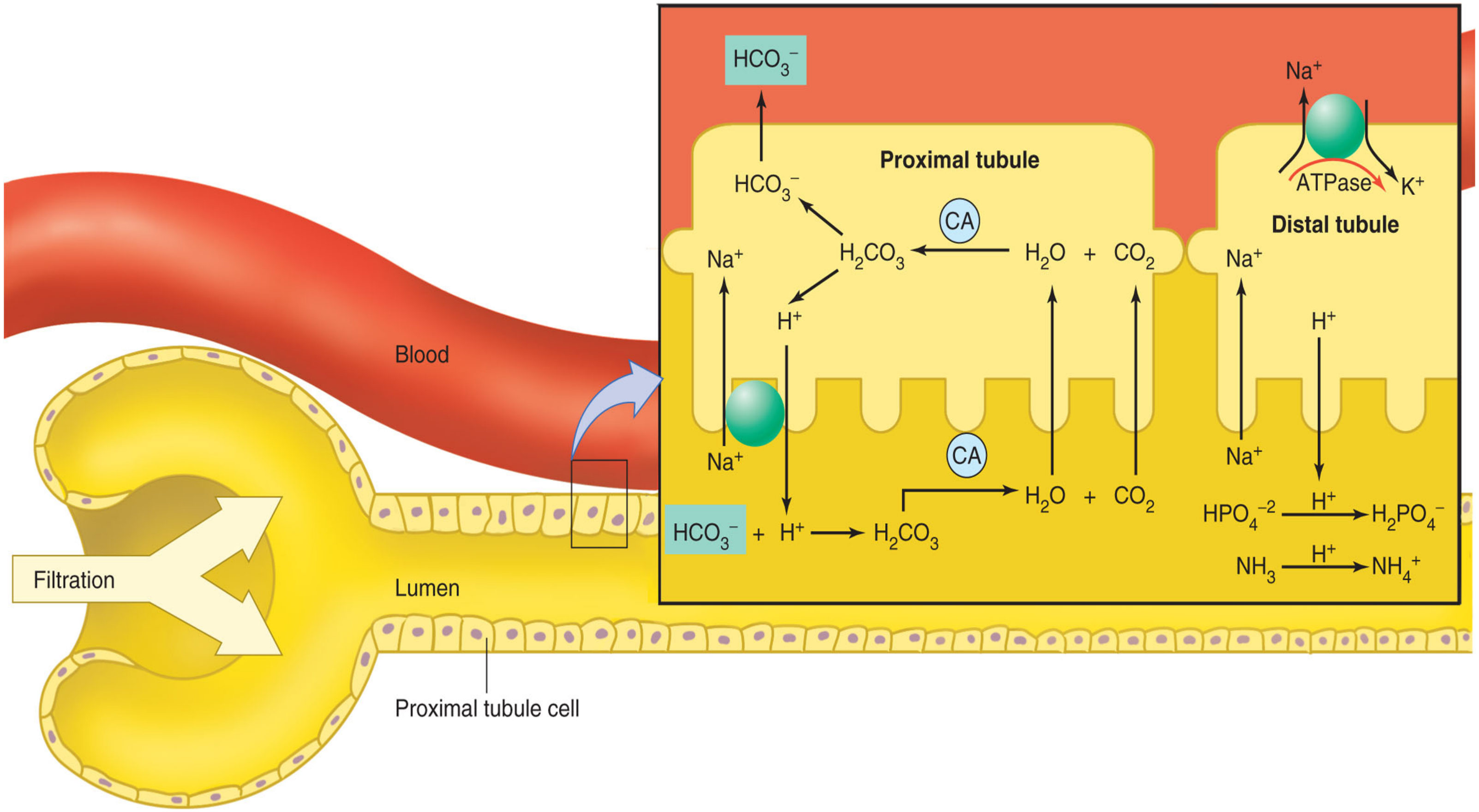
80-90% of Bicarbonate in urine reabsorbed as CO_2 from the lumen of the tubule

- Carbonic anhydrase on **lumenal surface** converts HCO_3^- & H+ to CO_2 which can diffuse into epithelium cells.

- Carbonic anhydrase **inside epithelium cells** converts CO_2 back to HCO_3^- & H+ for transport in the blood.

H+ ATPase pump also adds protons to urine, making urine acidic in spite of CO_2 reabsorption.

Figure 17.29



Blood
Filtration
Lumen
Proximal tubule cell
Proximal tubule
HCO_3^-
HCO_3^-
H_2CO_3
CA
H_2O + CO_2
Na^+
H^+
Na^+
CA
H_2O + CO_2
HCO_3^- + H^+ → H_2CO_3
Distal tubule
Na^+
ATPase
K^+
Na^+
H^+
Na^+
HPO_4^{-2} H^+ → $H_2PO_4^-$
NH_3 H^+ → NH_4^+