Renal Physiology

RENAL PHYSIOLOGY 1 – 6

Renal Physiology

RENAL PHYSIOLOGY 1 INTRO & RENAL ANATOMY

Functions of the Kidney

RAAS System

- Production of Urine
  - Removal of wastes
  - Fluid balance as part of long-term blood pressure regulation
  - Electrolyte balance and osmolarity regulation
  - pH balance
- Secondary endocrine organ
  - Erythropoietin
  - Renin
  - Vitamin D metabolism

mostly K, Na, Ca, Cl

Hydrogen and Bicarbonate concentration maintains 7.35 and 7.45

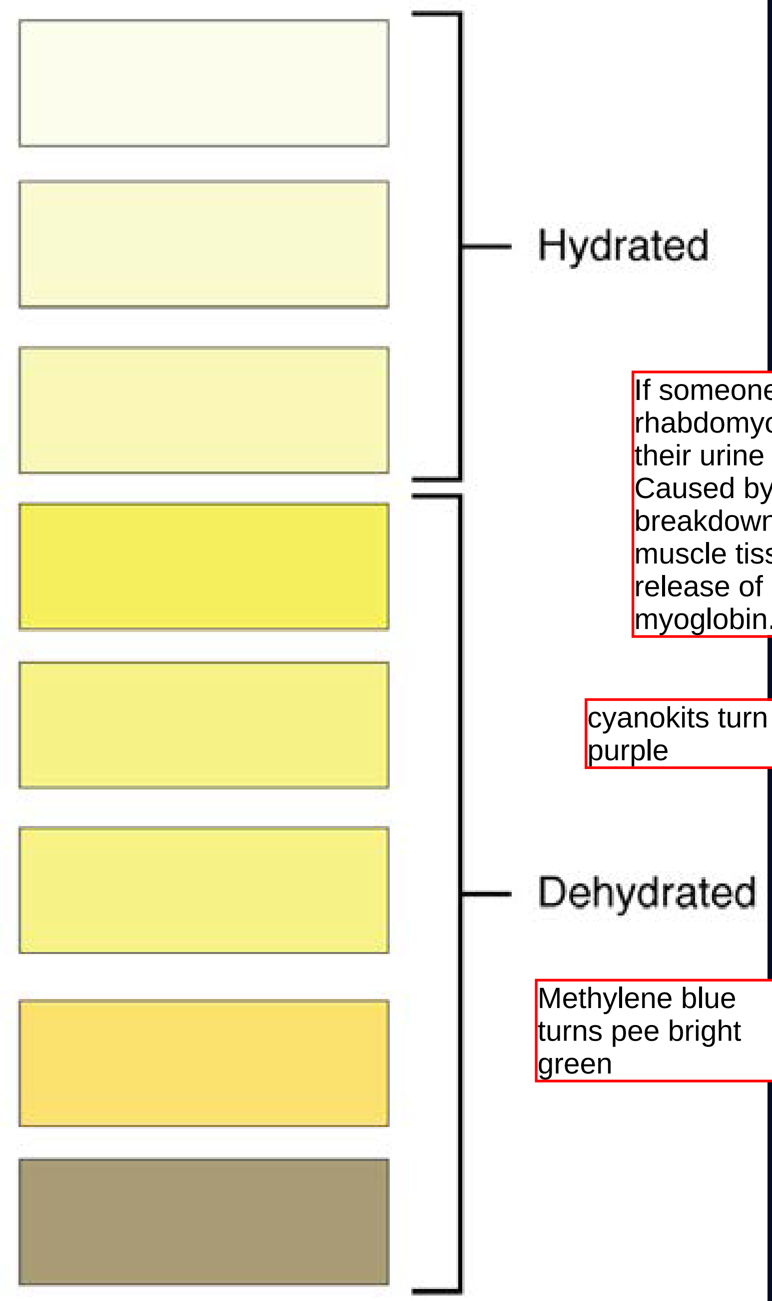
Hormone inducing erythroproiesis

Characteristics of Urine

Normal Urine Characteristics

Characteristic	Normal values
Color	Pale yellow to deep amber
Odor	Odorless
Volume	750–2000 mL/24 hour
pH	4.5–8.0
Specific gravity	1.003–1.032
Osmolarity	40–1350 mOsmol/kg
Urobilinogen	0.2–1.0 mg/100 mL
White blood cells	0–2 HPF (per high-power field of microscope)
Leukocyte esterase	None
Protein	None or trace
Bilirubin	<0.3 mg/100 mL
Ketones	None
Nitrites	None
Blood	None
Glucose	None

Table 25.1



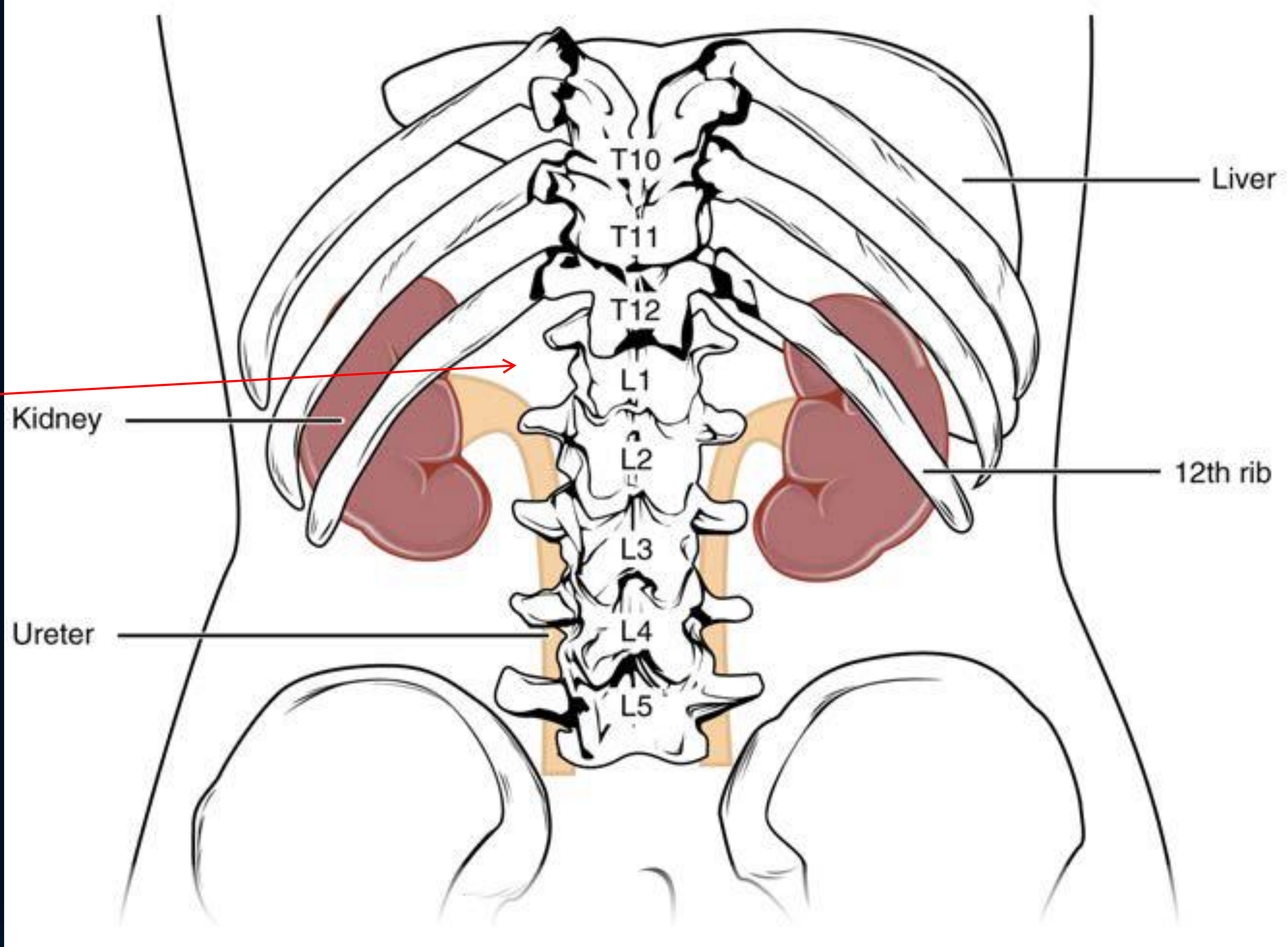
If someone has rhabdomyolysis, their urine is brown. Caused by breakdown of muscle tissue and release of myoglobin.

cyanokits turn pee purple

Methylene blue turns pee bright green

Location of the Kidneys

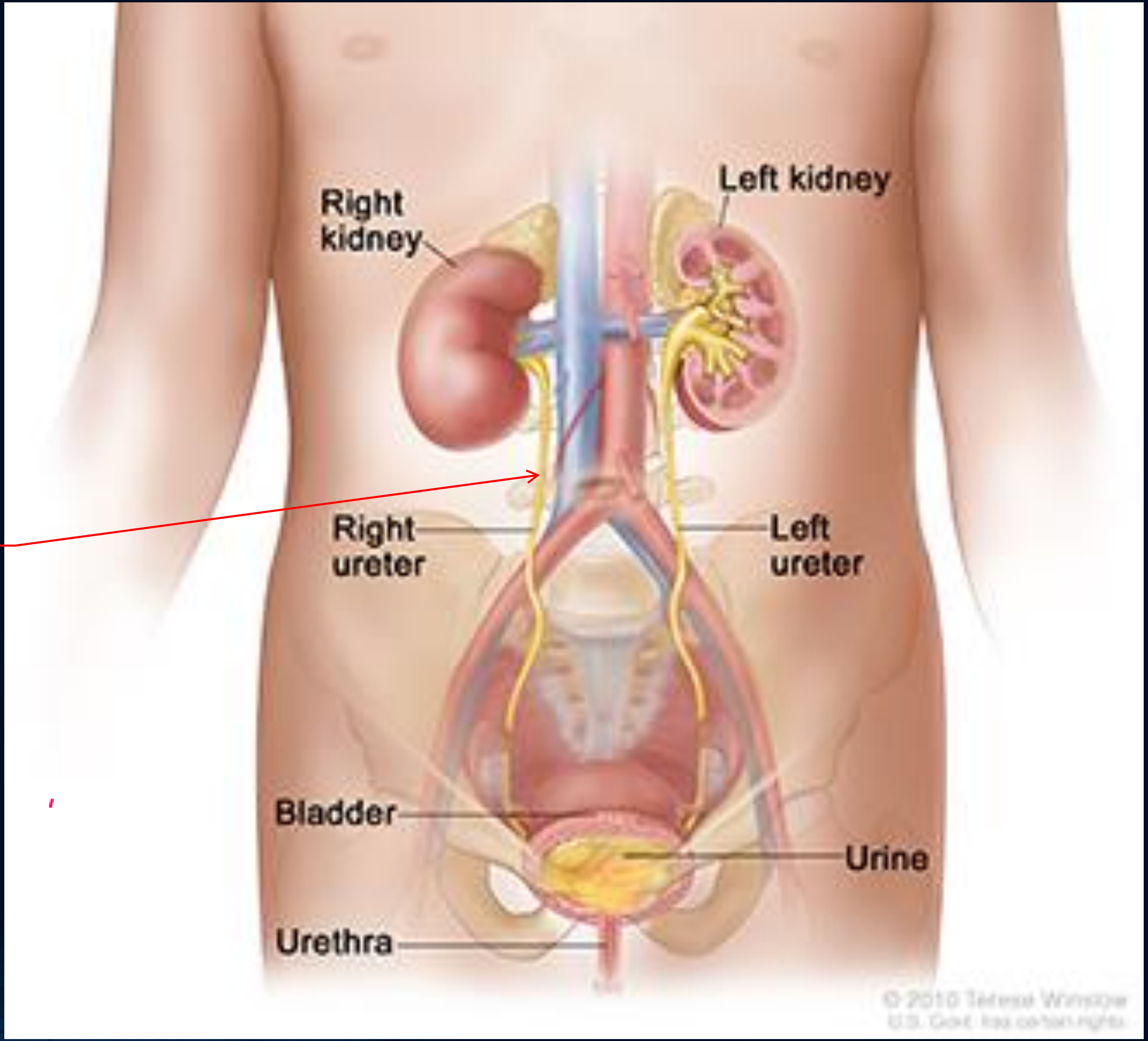
CSAC



Lies in the retroperitoneum

Kidney pain presents in the costovertebral angle (CSA).

Urinary System

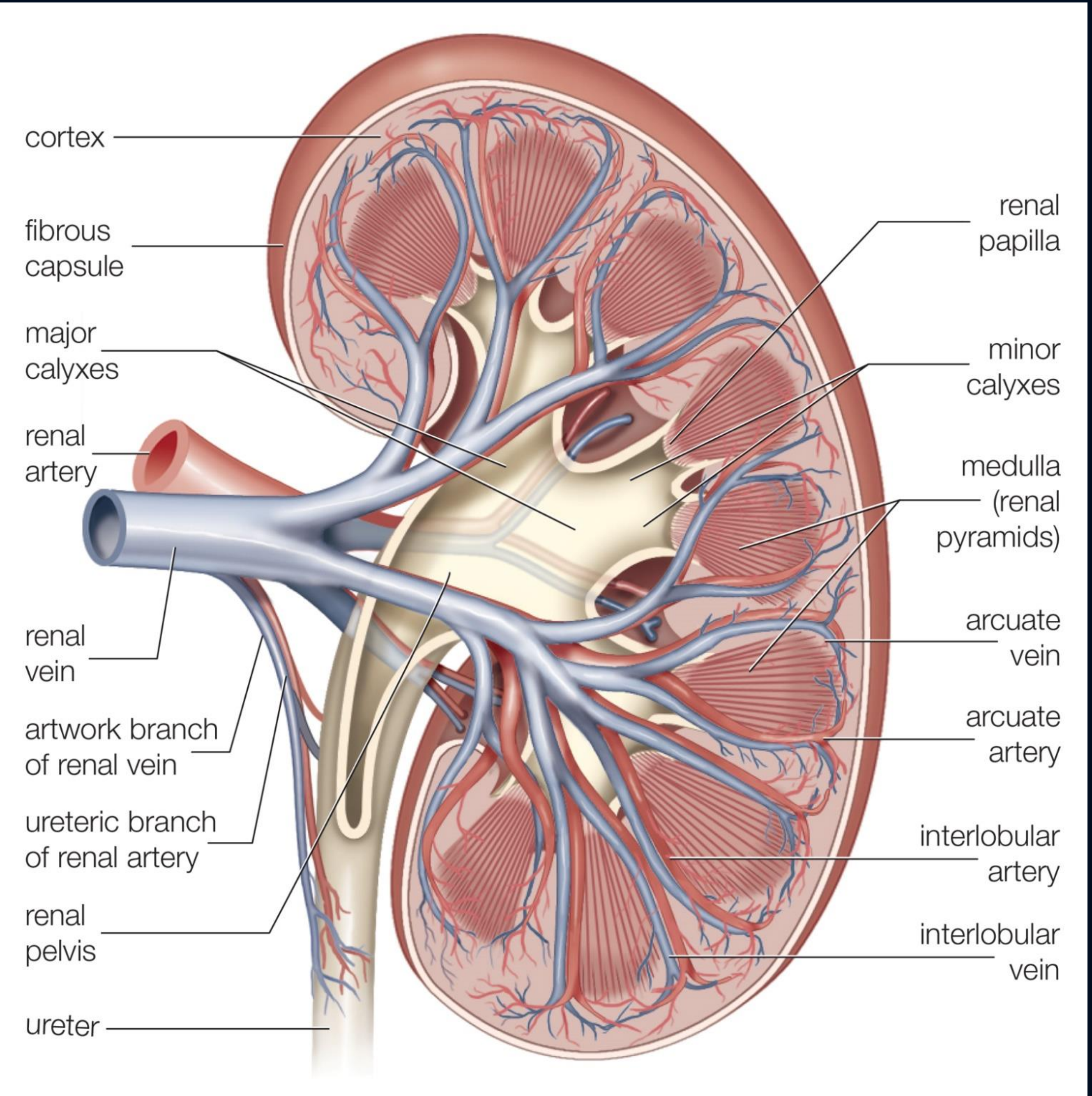


calcium kidney stones tear this apart, causing pain

Kidney injures present as hematuria, Grey Turner's sign (back/flank bruising)

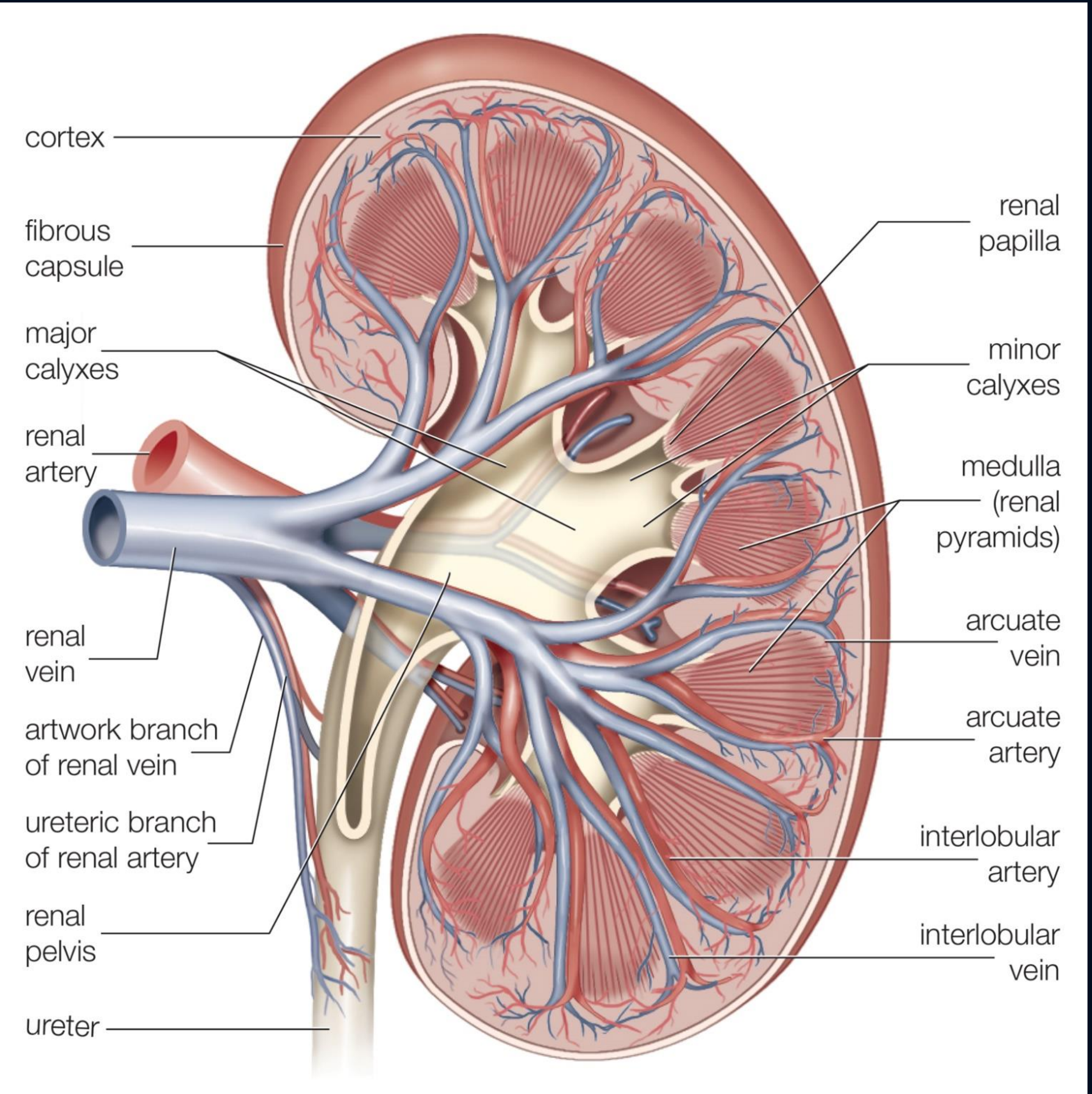
Kidney Anatomy

- Functional Unit = Nephron
  - 1 Million per Kidney
- 20% of Cardiac Output
- 180L of filtrate
- 99% reabsorbed
- >1cc/kg/hr - Normal
- <0.5cc/kg/hr - anuria

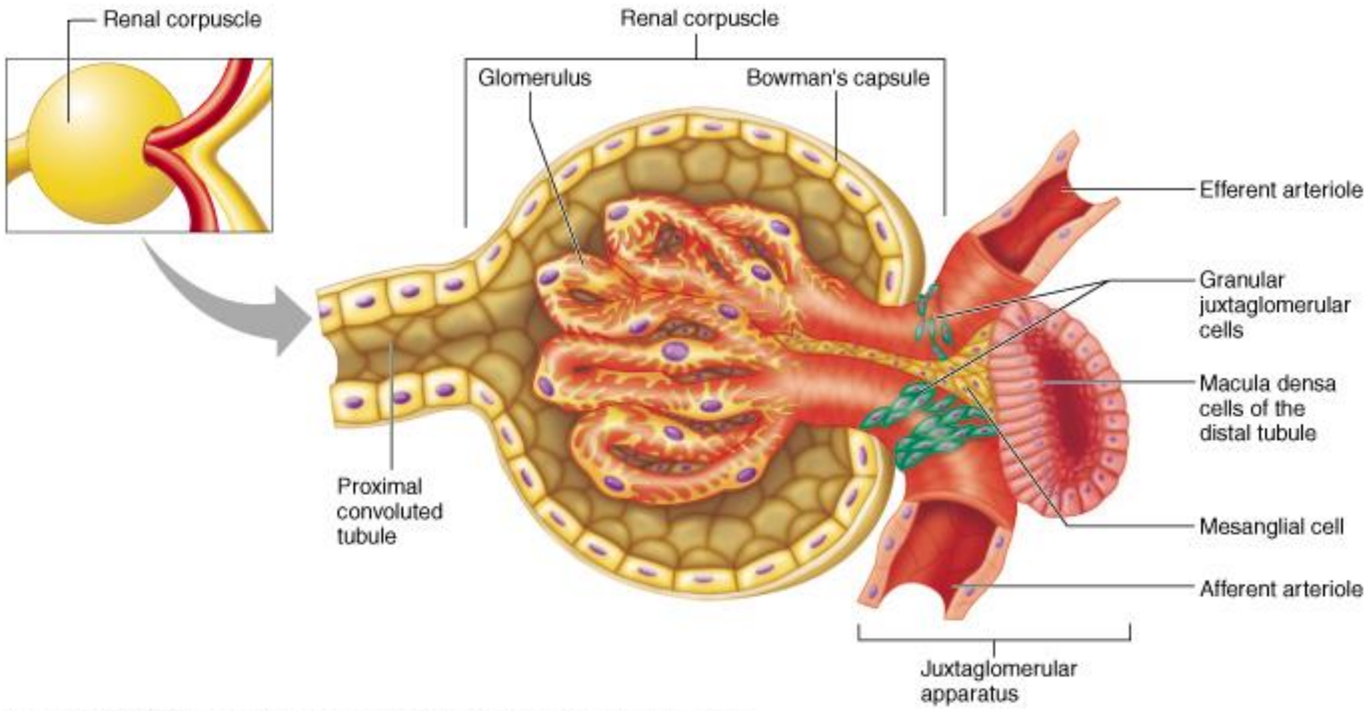


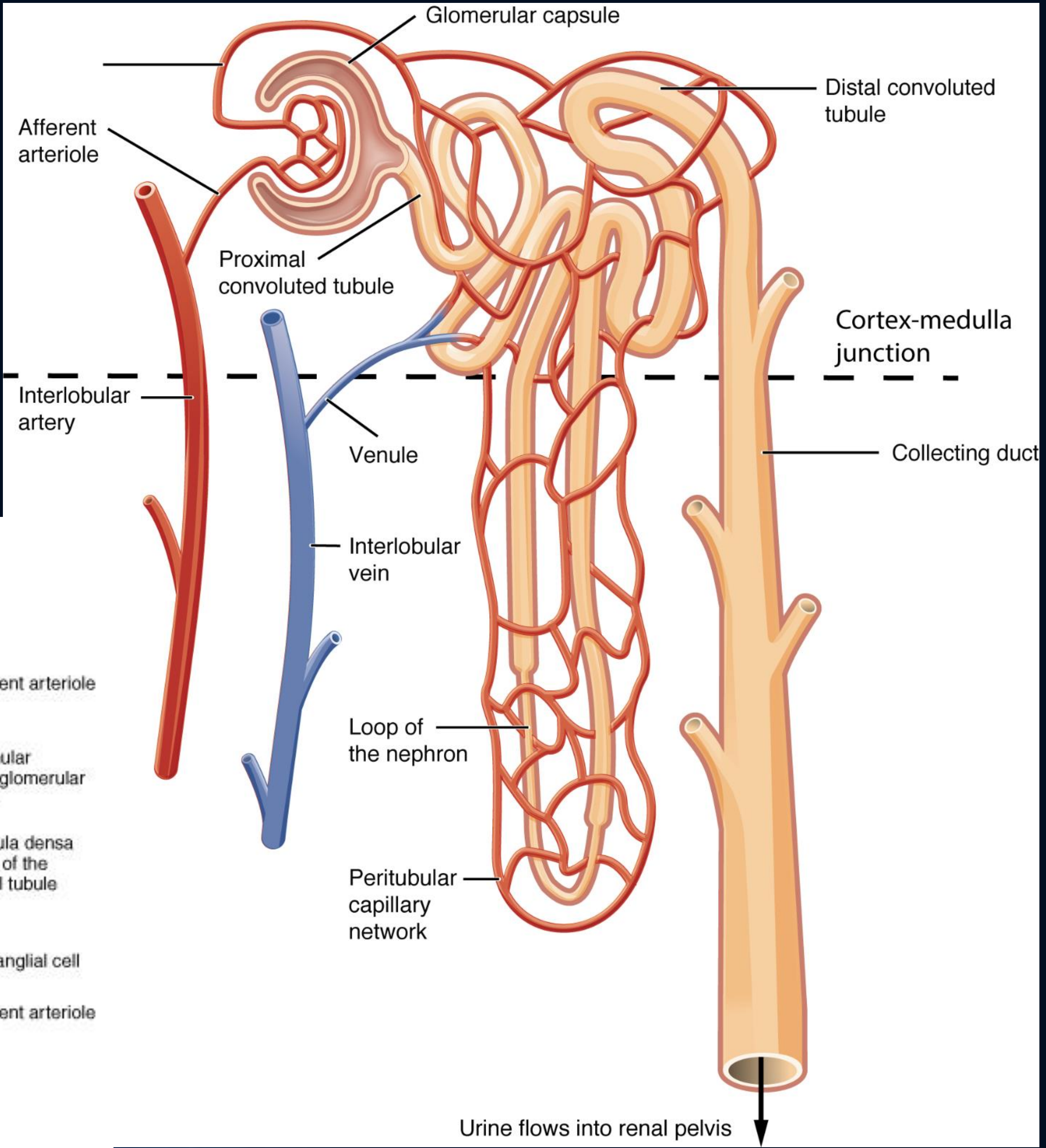
Kidney Anatomy

- Rt/Lt Renal A. --> Segmental A. --> Interlobular A. --> Arcuate A. --> Afferent A. --> Glomerulus --> Efferent A (peritubular V) --> Arcuate V --> Interlobular V --> Segmental V --> Renal V
- Nephrons Renal Pyramids Minor Calyx Major Calyx Renal Pelvis Ureter



Nephron Anatomy





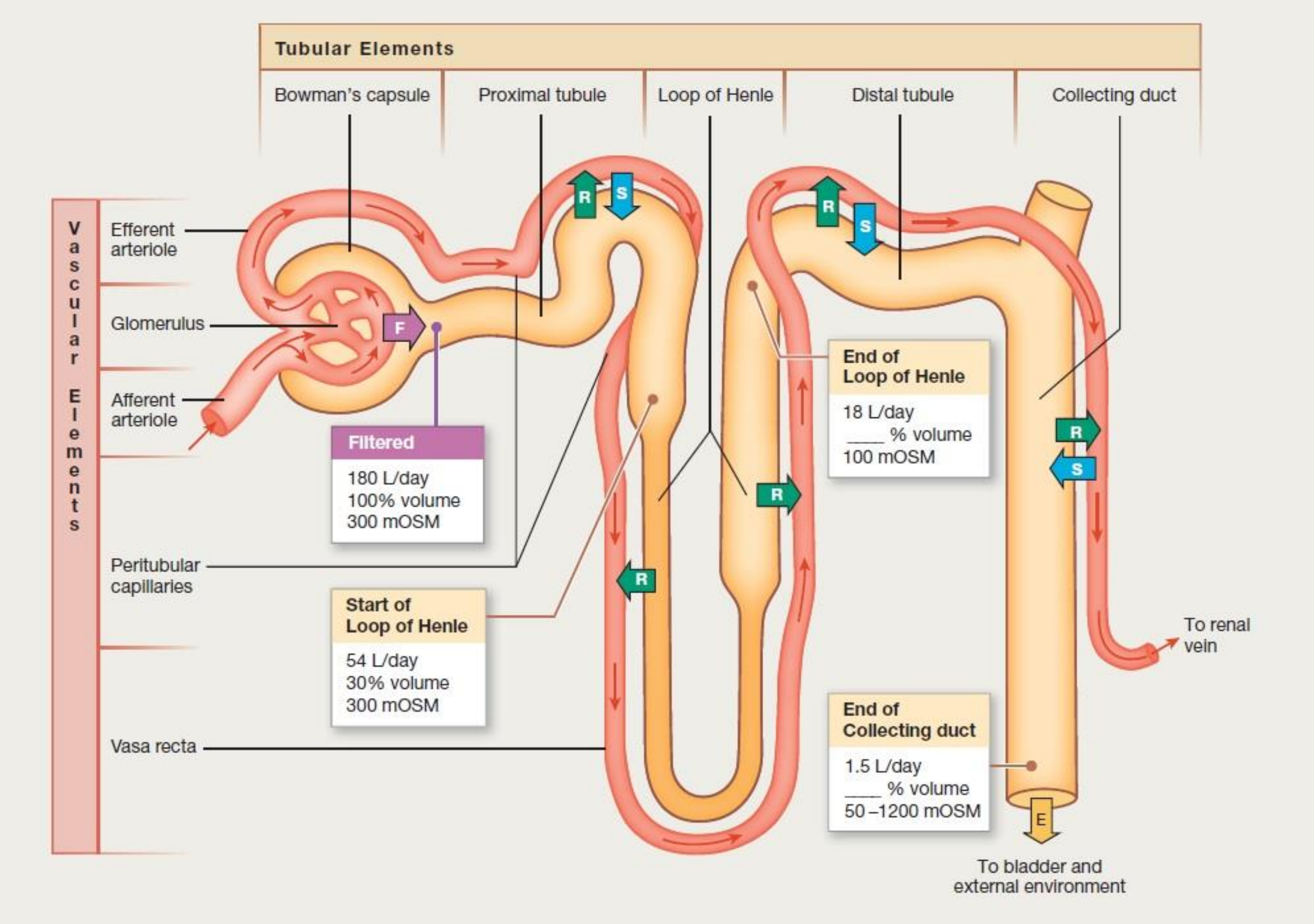
Nephron Key Functions

Filtration
- Glom → BC
- 20% CO (125ml/min)
- 180,000ml a day
- Glomerular Filtration Rate

Reabsorption
- Tubule → PTC
- 99% of filtrate
- Different amounts of solutes

Secretion
- PTC → Tubule

Excretion
- E = F – R + S



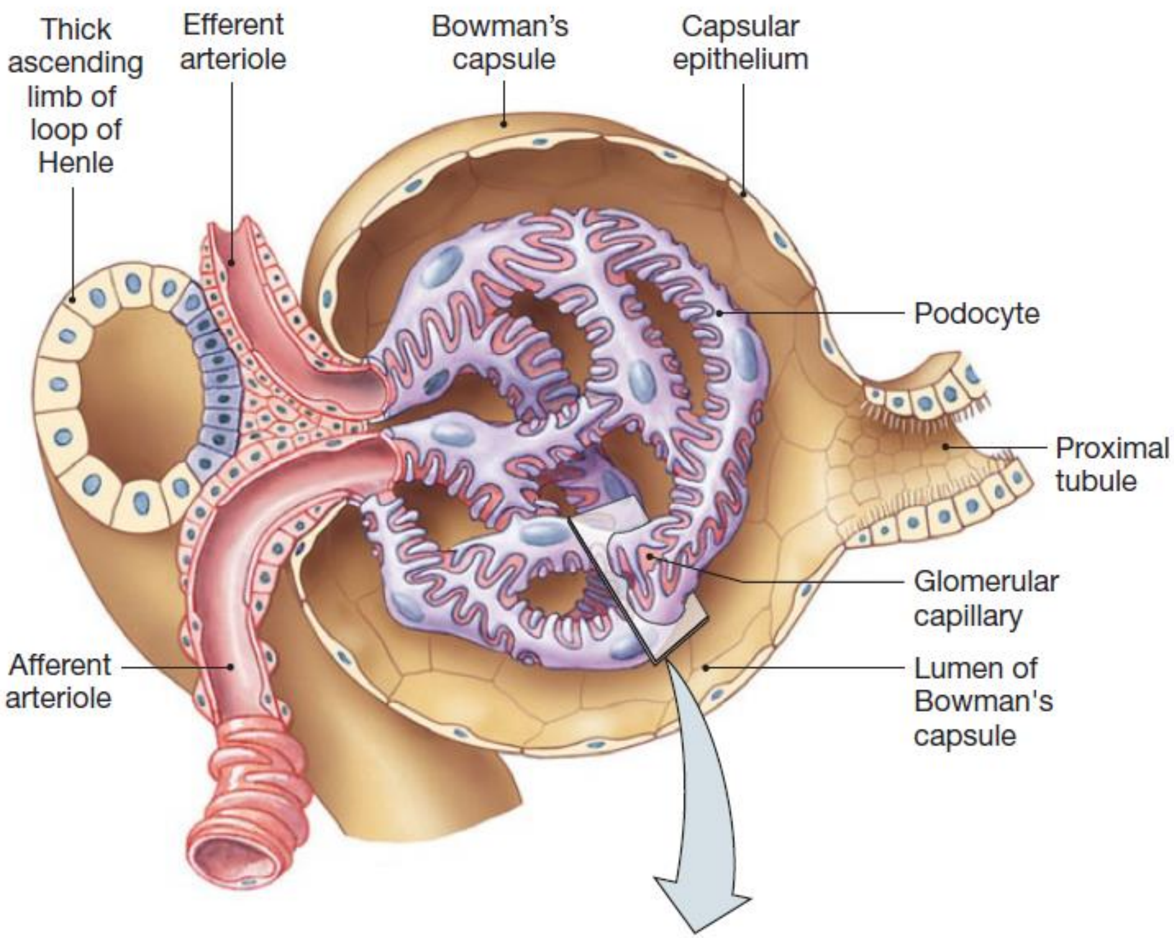
Renal Physiology

RENAL PHYSIOLOGY 2 FILTRATION

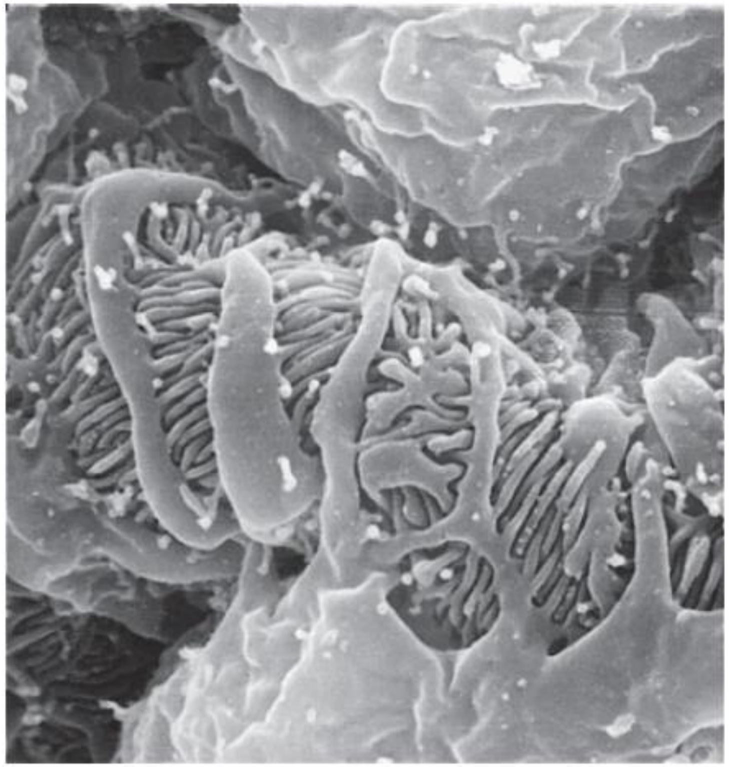
Renal Corpuscle = Glomerulus + BC

THE RENAL CORPUSCLE

(a) The epithelium around glomerular capillaries is modified into podocytes.

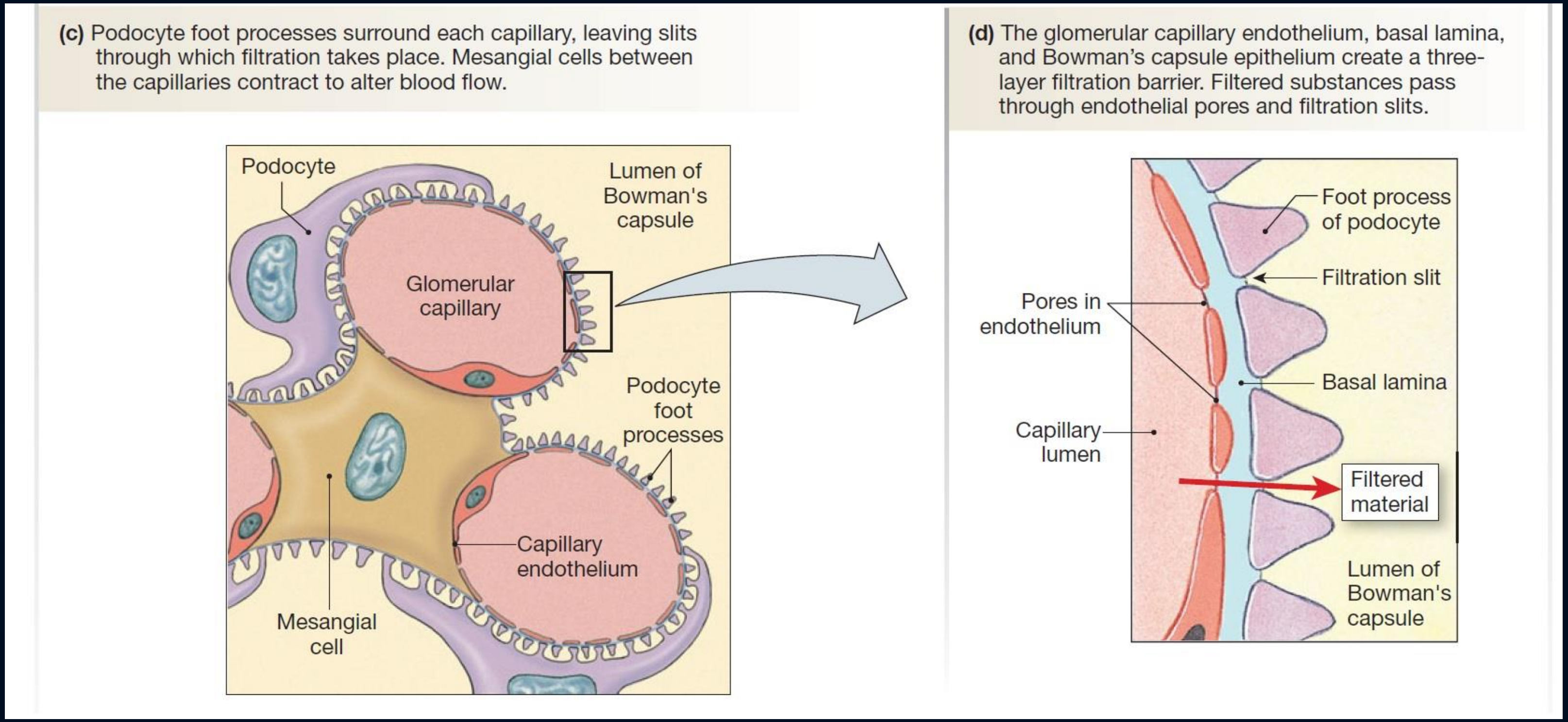


(b) Micrograph showing podocyte foot processes around glomerular capillary.

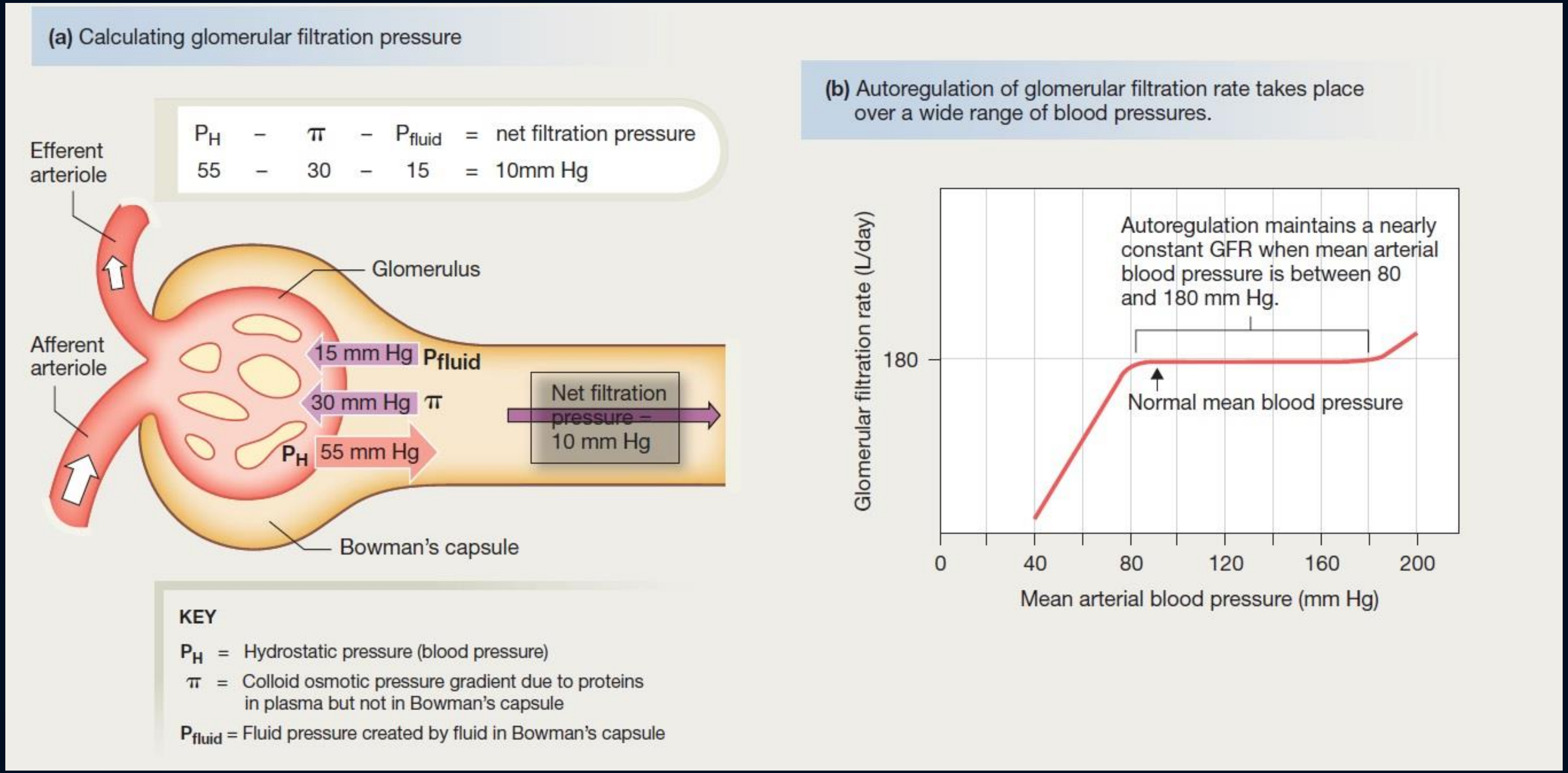


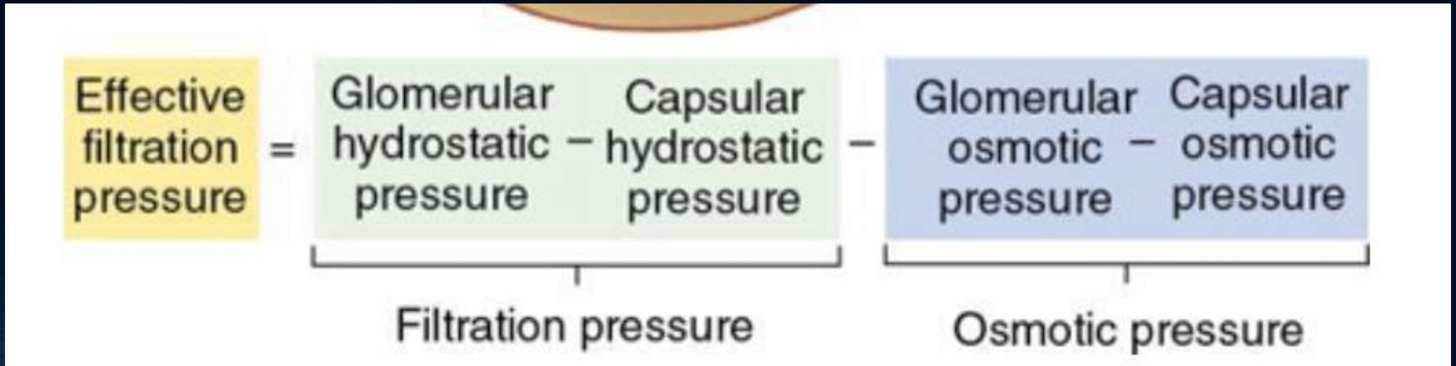
Filtration Barriers (Glomerular-Capsular Membrane)

1. Podocytes
   - Filtration Slits
   - Slit diaphragm
2. Glomerular Endothelium
   - Fenestrations
3. Basement Membrane
   - Negative Charge



Starling Forces



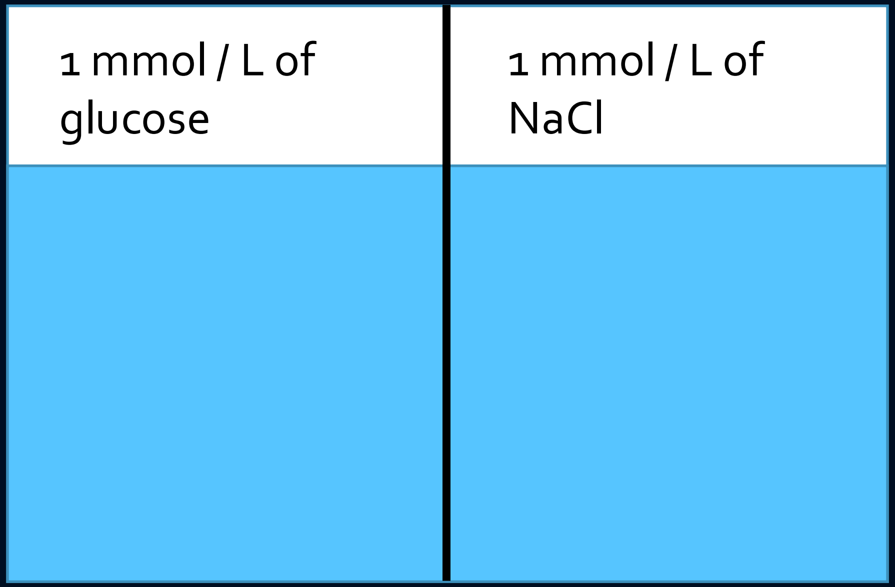


Glomerular Filtration Rate (GFR)

- Volume filtered per unit time of total blood
- Renal blood flow = CO x % of blood that goes to kidneys
- Renal plasma flow = RBF x 0.55 (proportion of blood that is plasma)
- GFR = RPF x 19% (amount of plasma that is actually filtered)
- GFR = 125 mL / min = 180 L / day

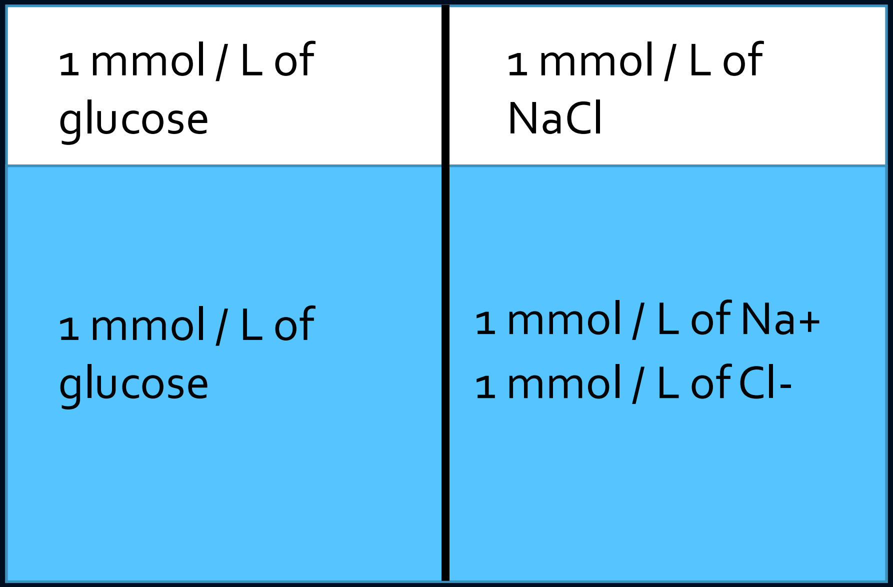
Osmolarity

- Osmolarity
  - Concentration of osmotically active particles (osmols) in a solution (mosmol / L)
  - How do osmoles differ from moles
    - Consider a 1 mmol / L solution of glucose and 1 mmol / L solution of NaCl, separated by a membrane that is permeable to water
    - What happens next?



Osmolarity

- Glucose does not dissociate is solution so 1 mmol / L
- NaCl dissociates into 1 mmol / L of Na+ and 1 mmol /L of Cl- thus the NaCl solution has 2 mmol / L of osmotically active particles or 2 mosmol / L
- Water will move toward the NaCl solution
- Under normal conditions, ECF and ICF have equal osmolarities → ~ 300 mosmol / L



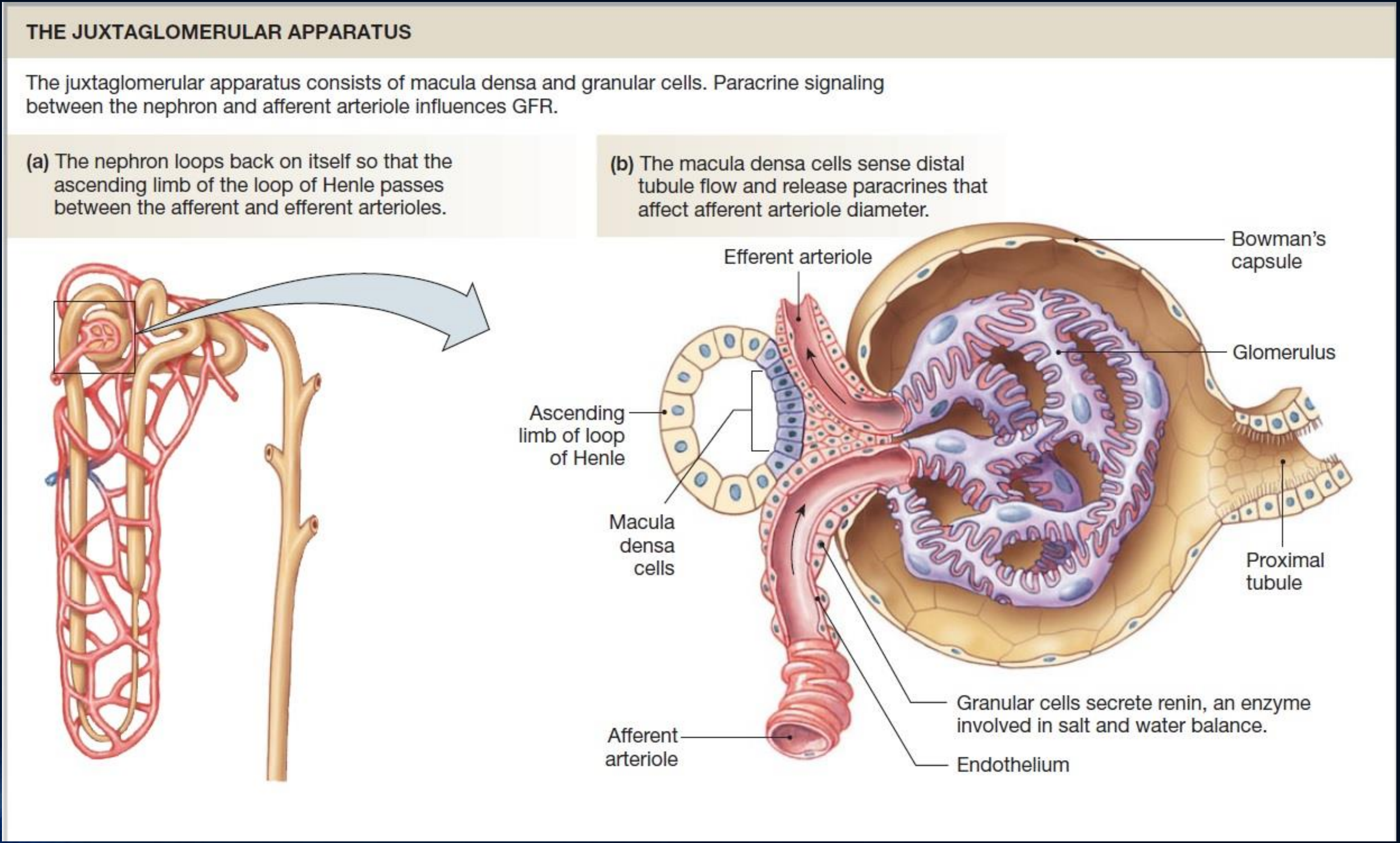
Composition of Filtrate

- Everything but blood cells and large plasma proteins <u>can</u> be filtered
- Approximately 20% of plasma is actually filtered
- Filtrate has osmolality of approximately 300 mosmol / L
- Blood leaving glomerulus to enter into efferent arteriole has a higher than normal osmolarity

Regulation of GFR

- Despite blood pressure changes, GFR is very stable at approximately 125 mL / min
- Mechanisms
- Autoregulation
  - Myogenic model
    - high pressure leads to higher blood flow through afferent arteriole which increases GFR
    - High blood pressure causes smooth muscle to stretch, opening VG Ca^{+2} channels
    - Ca^{+2} allows cross bridges to form promoting contraction of smooth muscle cells
    - This results in decreased GFR
    - When pressure decreases, smooth muscles relax, increasing blood flow and GFR
- Tubuloglomerular Feedback

JGA


THE JUXTAGLOMERULAR APPARATUS
The juxtaglomerular apparatus consists of macula densa and granular cells. Paracrine signaling between the nephron and afferent arteriole influences GFR.
(a) The nephron loops back on itself so that the ascending limb of the loop of Henle passes between the afferent and efferent arterioles.
(b) The macula densa cells sense distal tubule flow and release paracrines that affect afferent arteriole diameter.
Efferent arteriole
Bowman's capsule
Glomerulus
Ascending limb of loop of Henle
Macula densa cells
Proximal tubule
Granular cells secrete renin, an enzyme involved in salt and water balance.
Endothelium
Afferent arteriole

Regulation of GFR

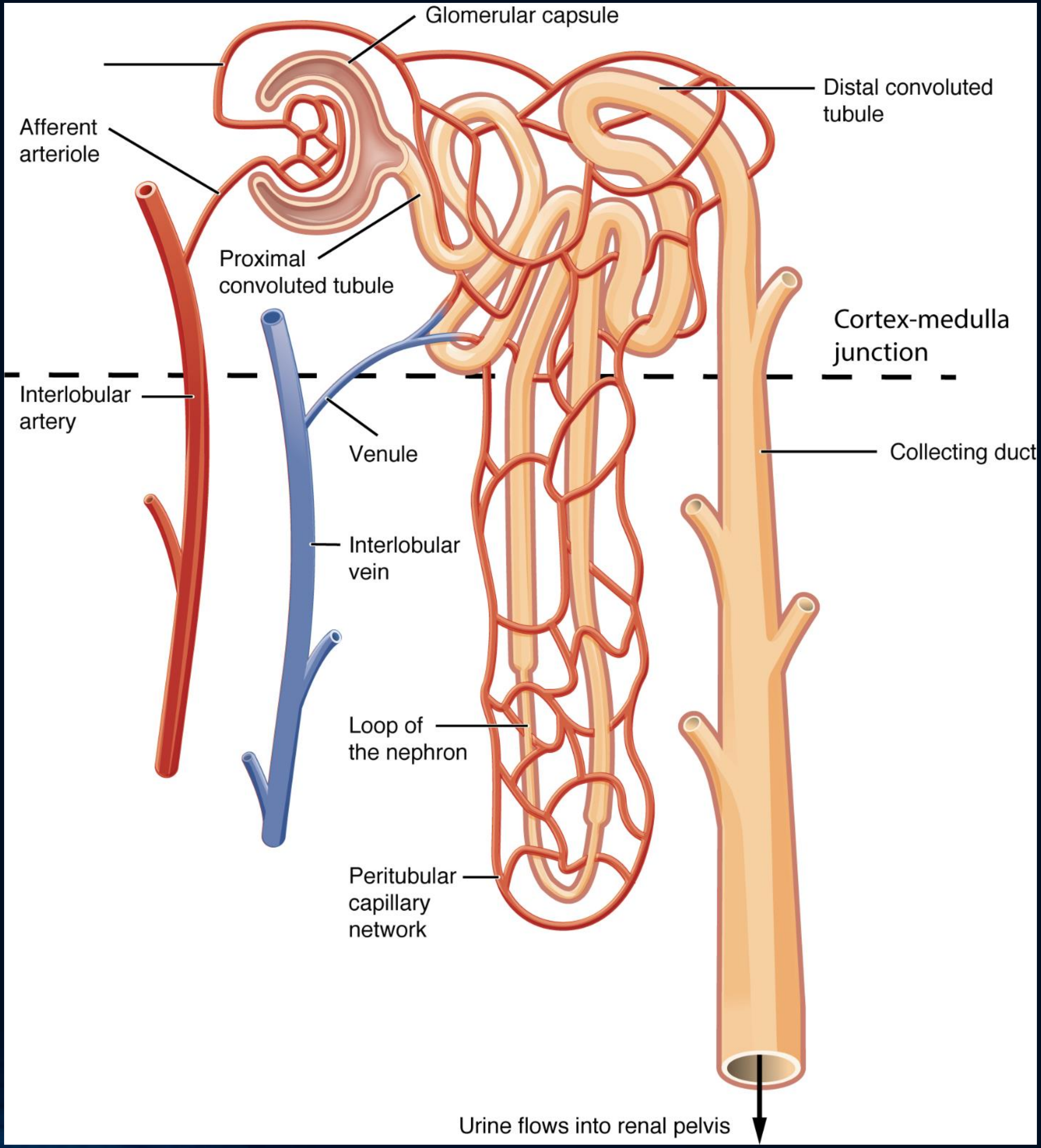
- Despite blood pressure changes, GFR is very stable at approximately 125 mL / min
- Mechanisms
- Autoregulation
- Tubuloglomerular Feedback
  - Increased blood flow through afferent arteriole increases GFR and increases flow of filtrate through the nephron
  - Increased flow is sensed by macula densa cells of JGA
  - Macula densa cells secrete more of paracrine factors adenosine and ATP which cause smooth muscle cells of afferent arteriole to contract which decreases GFR; secrete less NO
  - When blood flow is decreased through afferent arteriole, macula densa cells secrete less adenosine and ATP and more NO
  - Permeability of glomerulus can also be altered by Angiotensin II (Ang II)

Renal Physiology

RENAL PHYSIOLOGY 3 REABSORPTION PCT

Proximal Convoluted Tubule

- Approximately 70% of reabsorption of water and solutes occurs at this part of the nephron
- Filtrate entering PCT has osmolarity of 300 mosm / L
- PCT composed of single layer of cuboidal epithelial cells
- Apical side (facing lumen of nephron) and basal side (facing interstitial space) are different in their expression of channels and transporters
- Most reabsorption involves the movement of Na+ and depends on concentration gradients



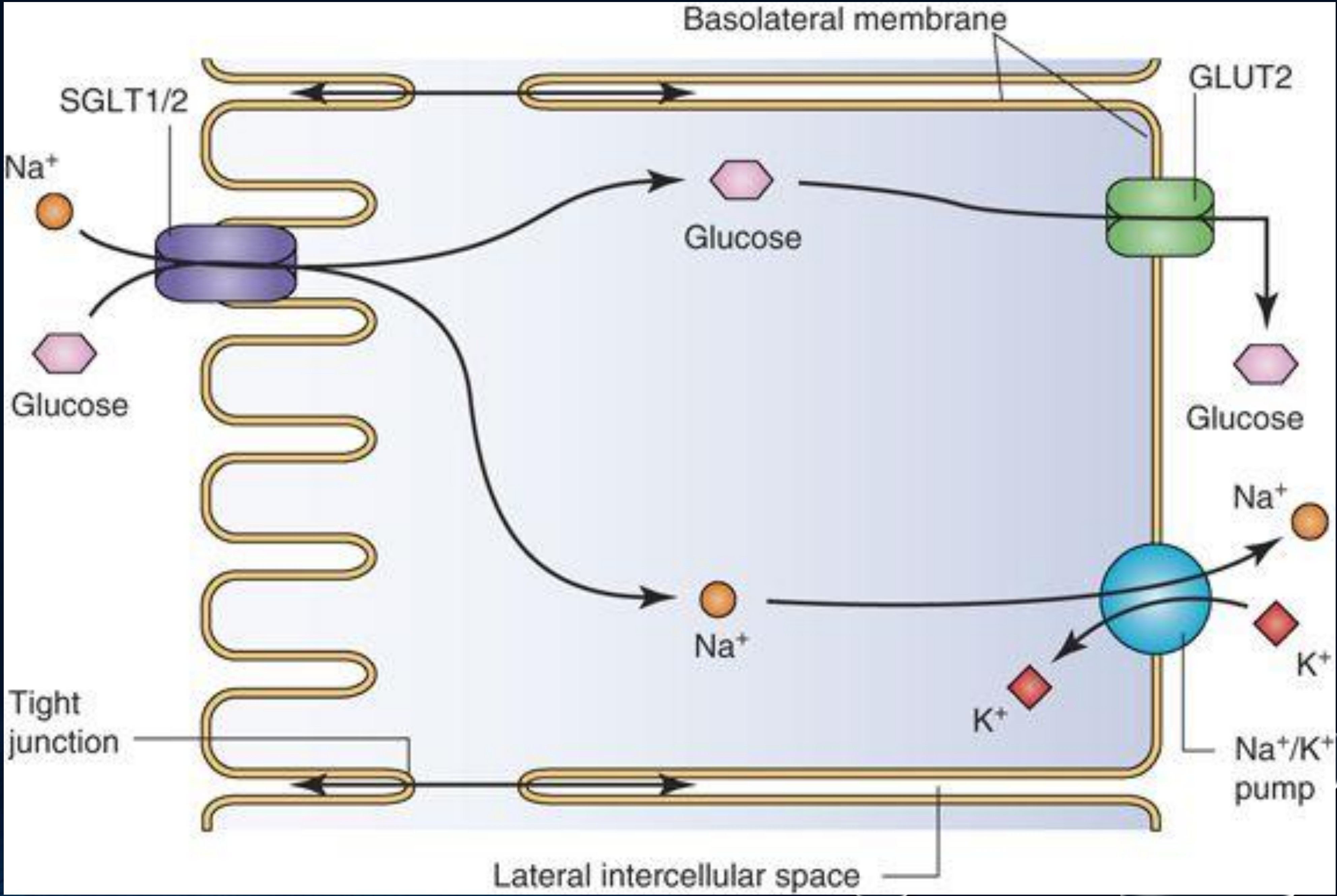
Reabsorption at Proximal Convoluted Tubule

- Transcellular mechanisms
  - Depend on Na+ gradients and supporting transport proteins

- Secondary active transport (ie glucose transport)
  - Facilitated diffusion on apical side
  - Active transport on basal side maintains the Na+ concentration gradient

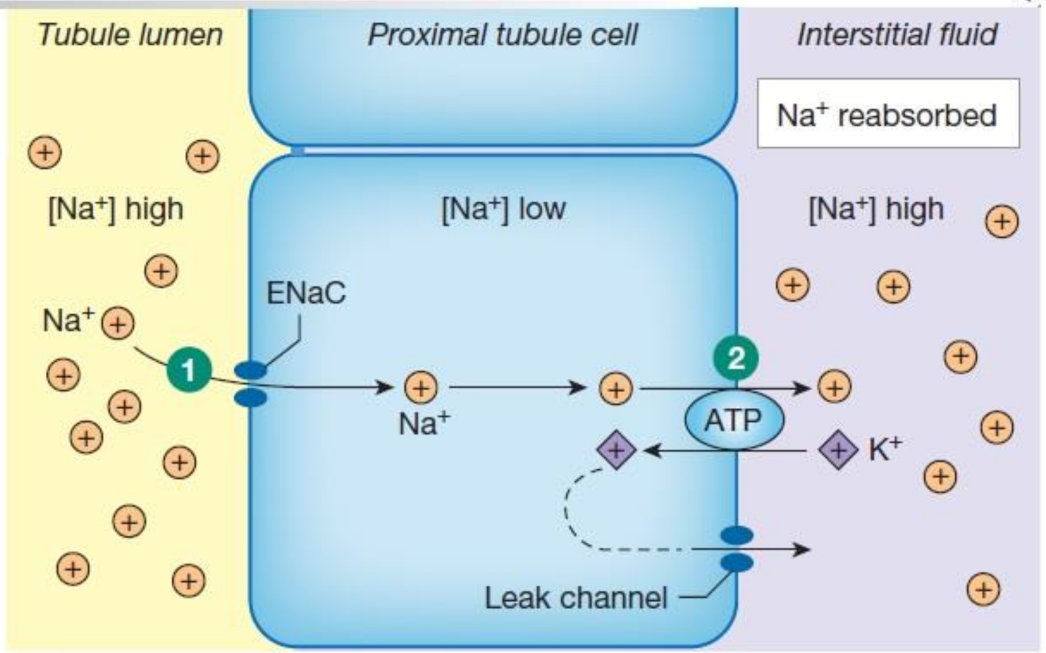
- Paracellular Mechanisms
  - Water follows the bulk of osmotically active particles by travelling between cells
  - Starling Forces in PCT favour movement of water from lumen of nephron to peritubular capillaries due to high osmotic pressure of the capillary

Secondary Active Transport in PCT



(b) Sodium reabsorption in the proximal tubule: active transport

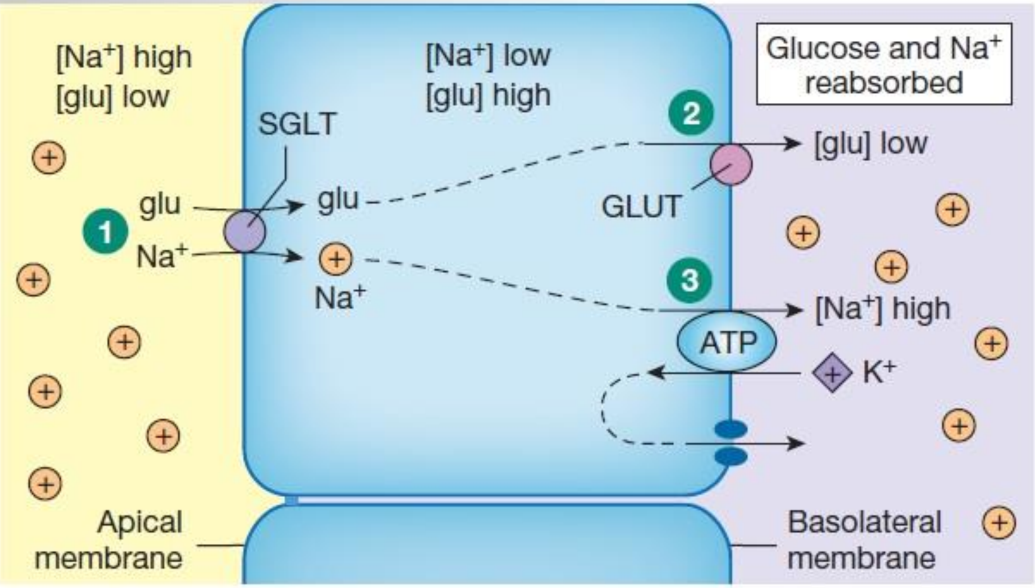
This figure shows the epithelial Na^+ channel, ENaC.



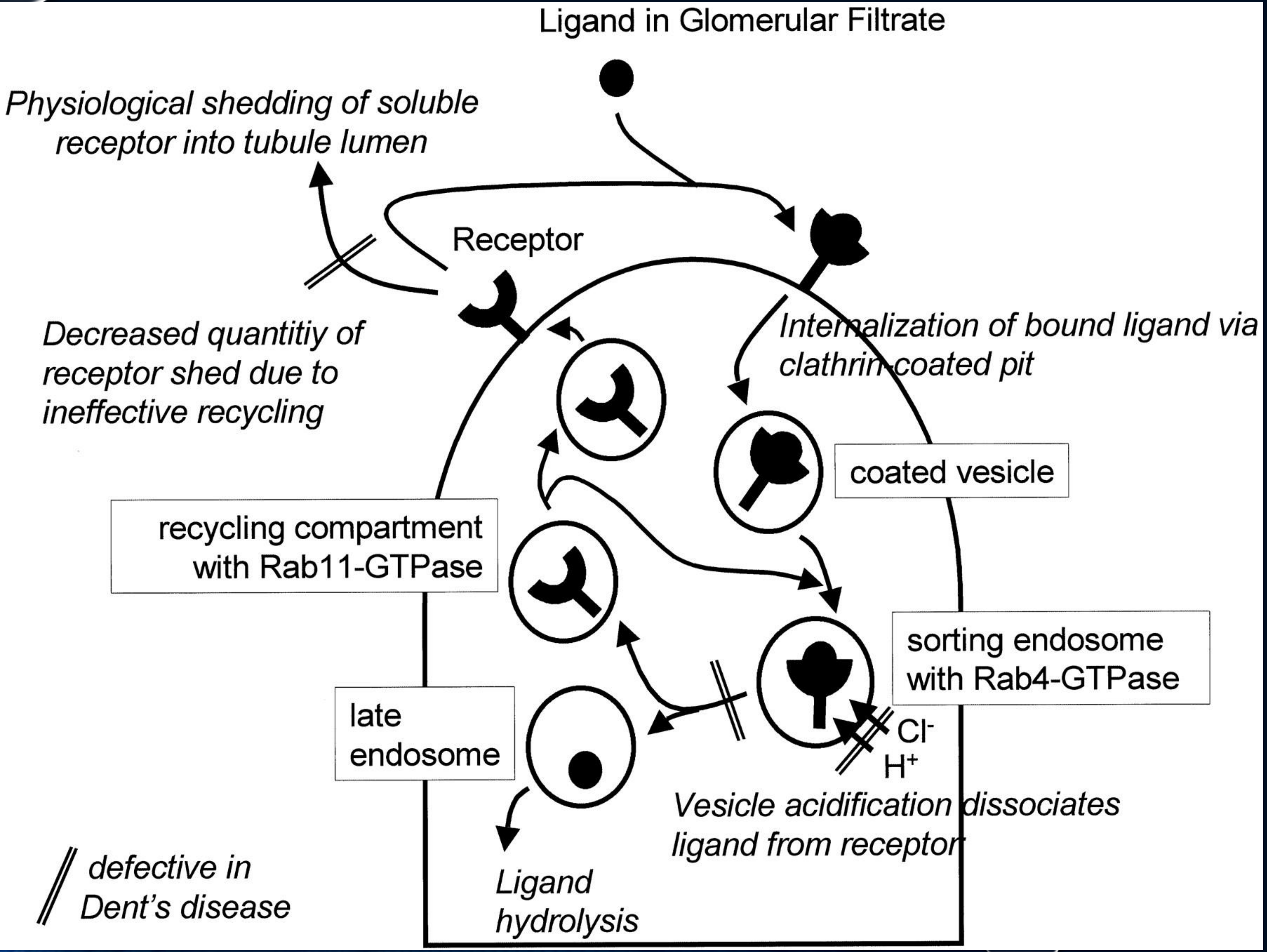
1. Na^+ enters cell through various membrane proteins, moving down its electrochemical gradient.
2. Na^+ is pumped out the basolateral side of cell by the Na^+-K^+-ATPase.

(c) Sodium-linked reabsorption: indirect (secondary) active transport

This figure shows glucose, but amino acids, other organic metabolites, and some ions such as phosphate are also absorbed by Na^+-dependent cotransport.



1. Na^+ moving down its electro-chemical gradient uses the SGLT protein to pull glucose into the cell against its concentration gradient.
2. Glucose diffuses out the basolateral side of the cell using the GLUT protein.
3. Na^+ is pumped out by Na^+-K^+-ATPase.


Ligand in Glomerular Filtrate
Physiological shedding of soluble receptor into tubule lumen
Receptor
Decreased quantitiy of receptor shed due to ineffective recycling
Internalization of bound ligand via clathrin-coated pit
coated vesicle
recycling compartment with Rab11-GTPase
sorting endosome with Rab4-GTPase
late endosome
Cl-
H+
Vesicle acidification dissociates ligand from receptor
Ligand hydrolysis
defective in Dent's disease

Receptor mediated endocytosis – recycling small peptides like renin and Ang II