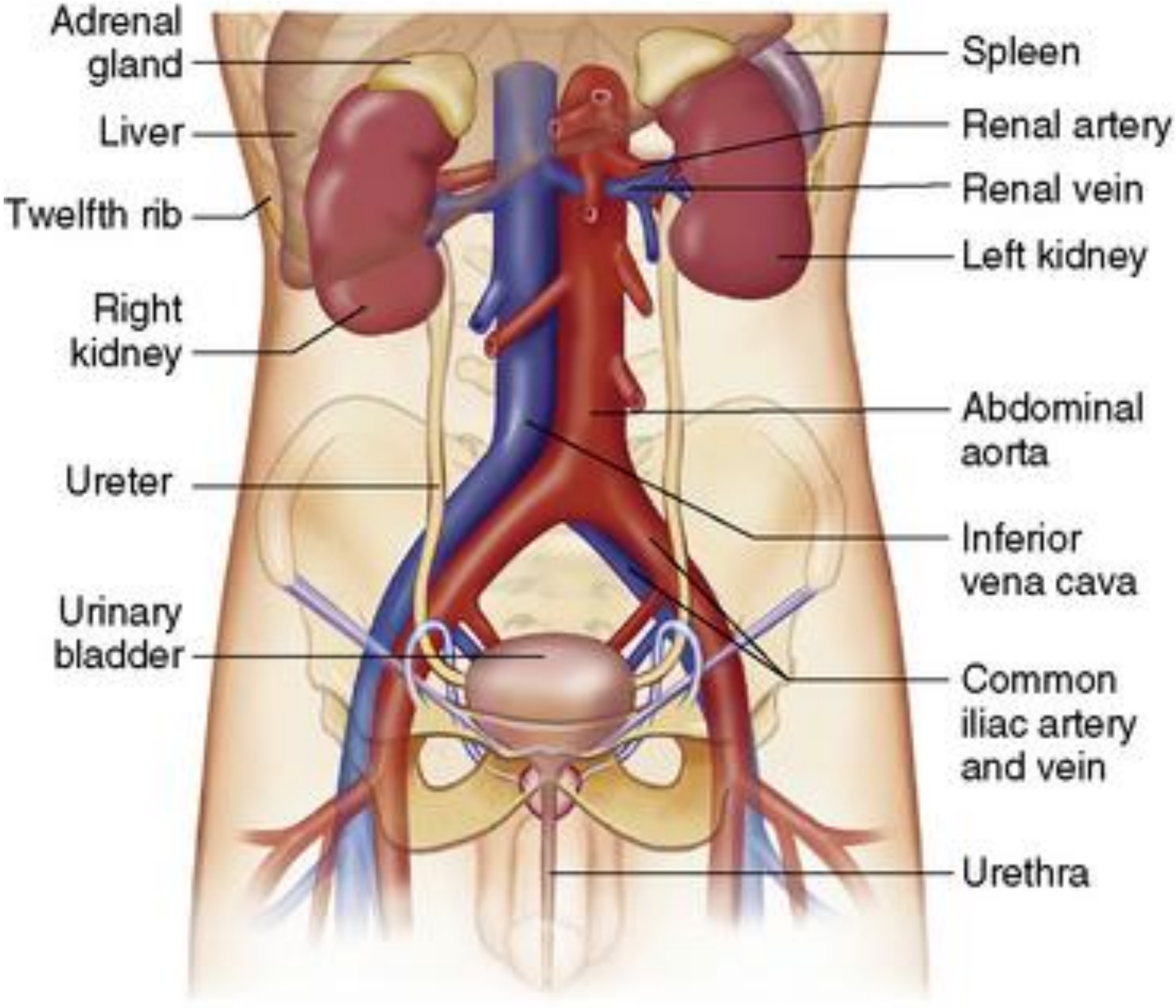
The Urinary system

Neelamshobha Nirala

Urinary (Renal) system

The kidney filters waste materials of blood and excrete them into fluid called Urine.

Once formed urine passes through ureters and is stored in urinary bladder until it excreted from the body through urethra.

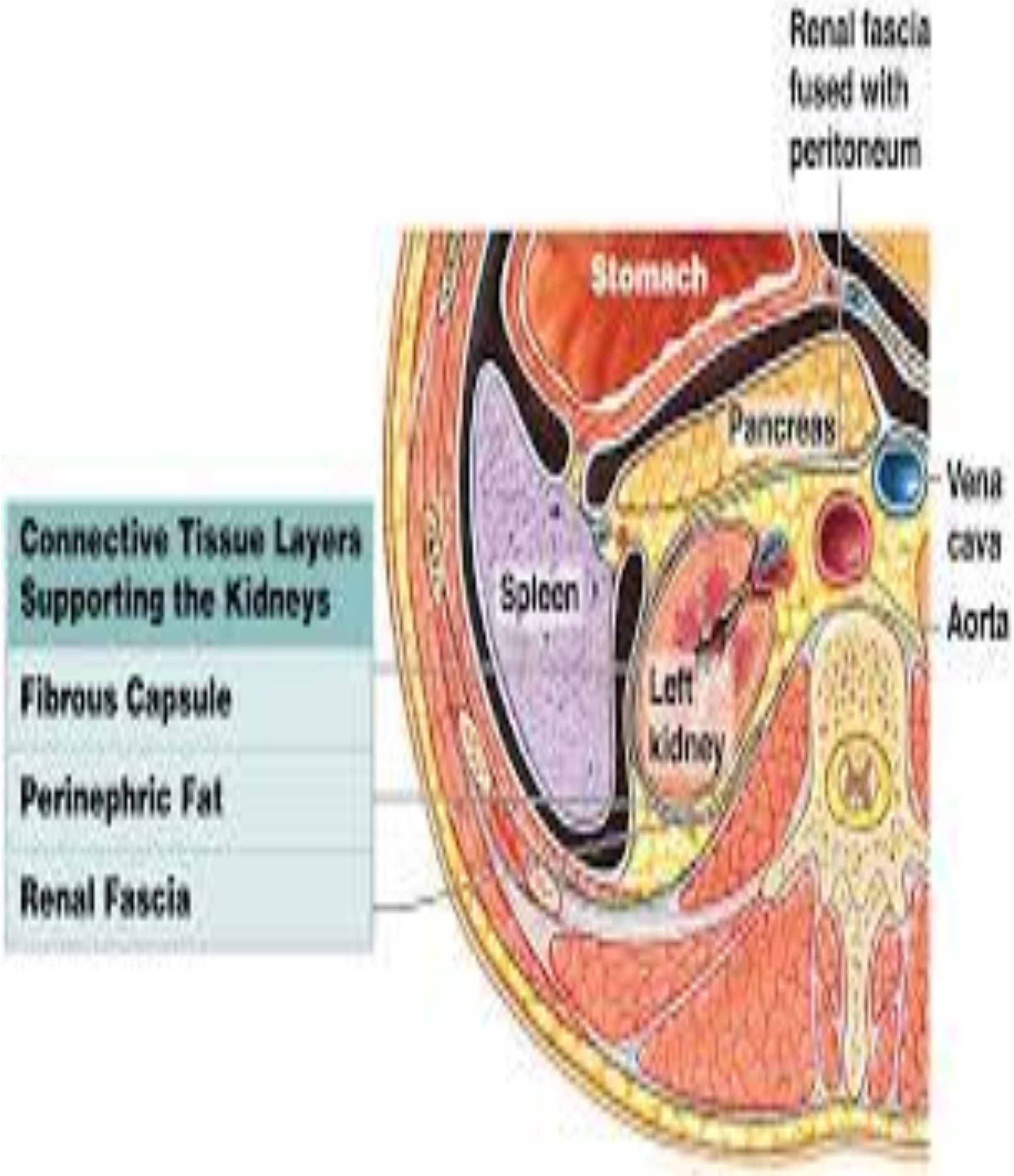


Functions of kidneys

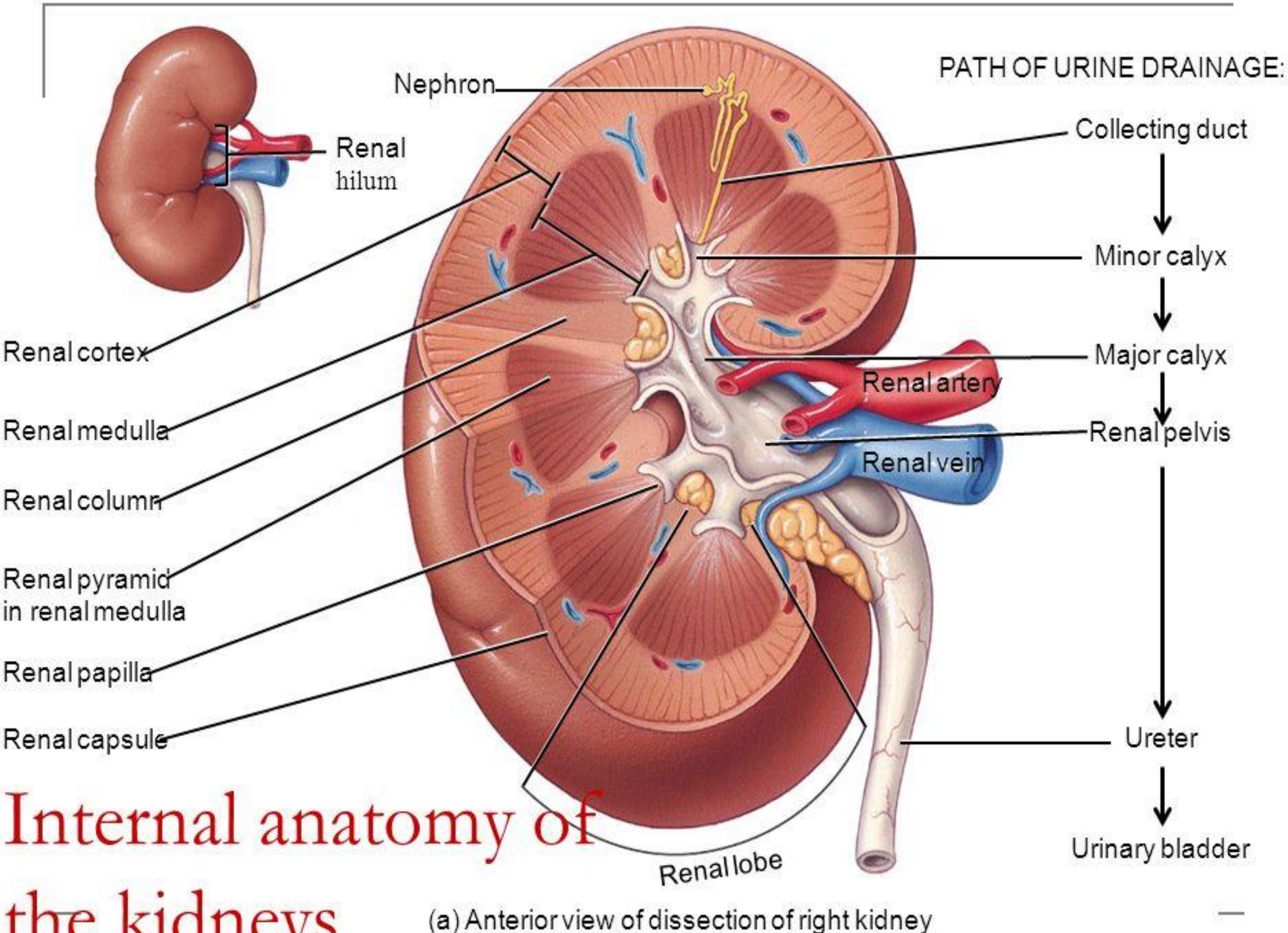
- Excretion of wastes: Nitrogenous wastes
  - Amino acid-> Urea and Ammonia
  - Creatinine Phosphate -> Creatinine
  - Nucleic acid -> Uric acid
  - Hemoglobin -> Urobilin
- Regulation of blood pH: excretion of H+
- Regulation of blood ionic composition: Na^+, K^+, Ca^{++}, Cl^-, HPO_4^{--}
- Regulation of blood volume:
- Regulation of blood pressure: by secreting renin
- Maintenance of blood osmolarity
- Production of hormones: Calcitriol and erythropoietin
- Regulation of blood glucose: Use amino acid glutamine in gluconeogenesis

Anatomy of kidney

- Reddish bean shaped organ, located just above the waist between peritoneum and the posterior wall of the abdomen.
- It is located between the levels of last thoracic and 3rd lumber vertebra, a position where they are partially protected by 11th and 12th ribs.
- Layers of kidney: it consists of 3 layers:
  - Renal Capsule: the innermost layer, is a smooth transparent sheet of dense irregular connective tissue that is continuous with the outer coat of the ureter. It works as barrier against trauma and helps to maintain the shape.
  - Adipose capsule: it is a mass of fatty tissue. It protects and hold the kidney.
  - Renal Fascia: a thin layer of dense irregular connective tissue that anchors the kidney in surrounding structures.



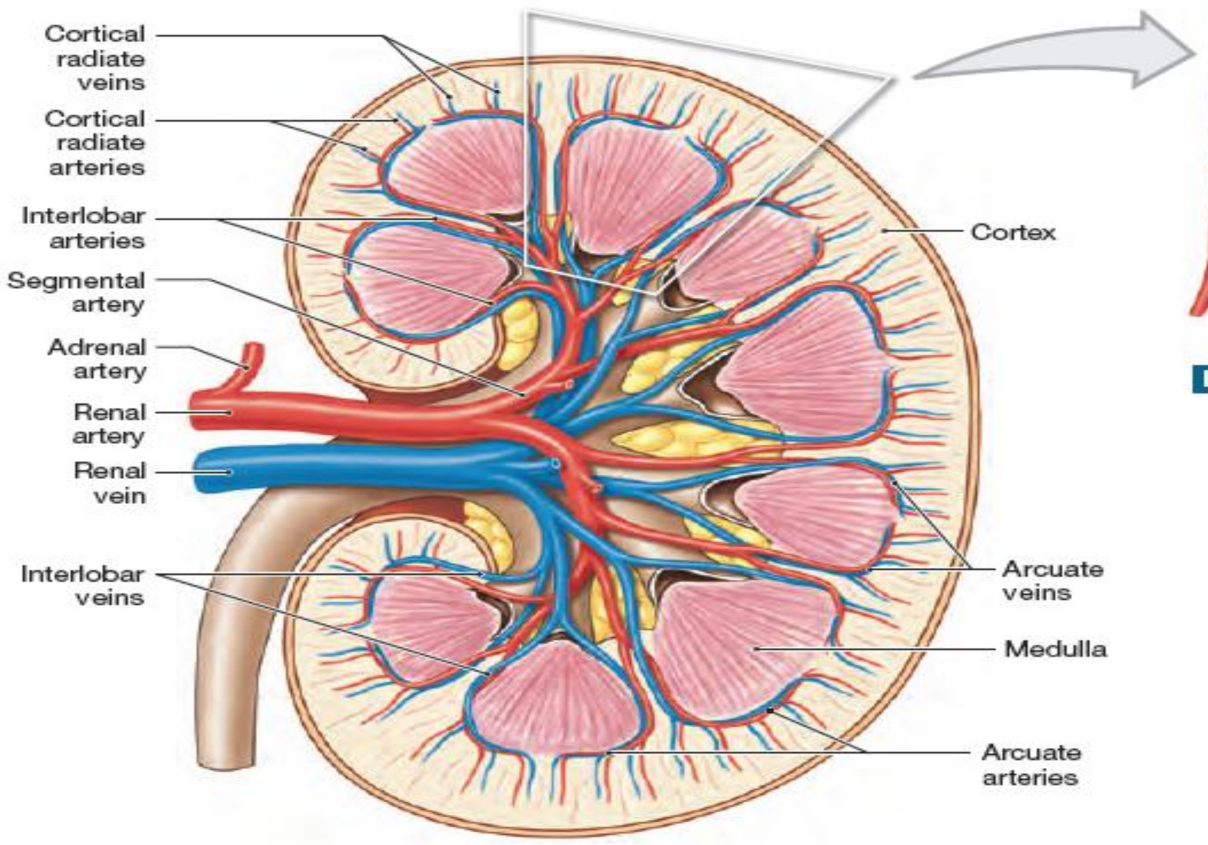
- Renal Cortex
- Renal medulla
    - Renal pyramid
    - Renal column
    - Renal papilla
- Together they form parenchyma : functional portion of the kidney as it contains nephron.
- Renal sinus: renal pelvis, calyces, and branches of renal blood vessels.



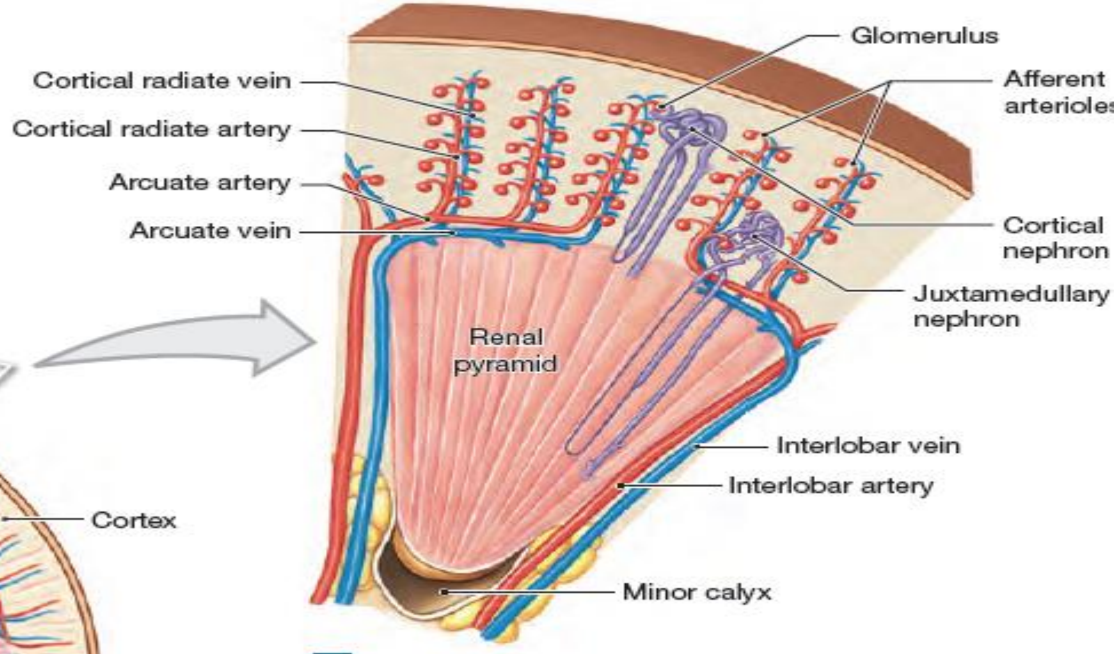
Internal anatomy of the kidneys

Blood and nerve supply of the kidney

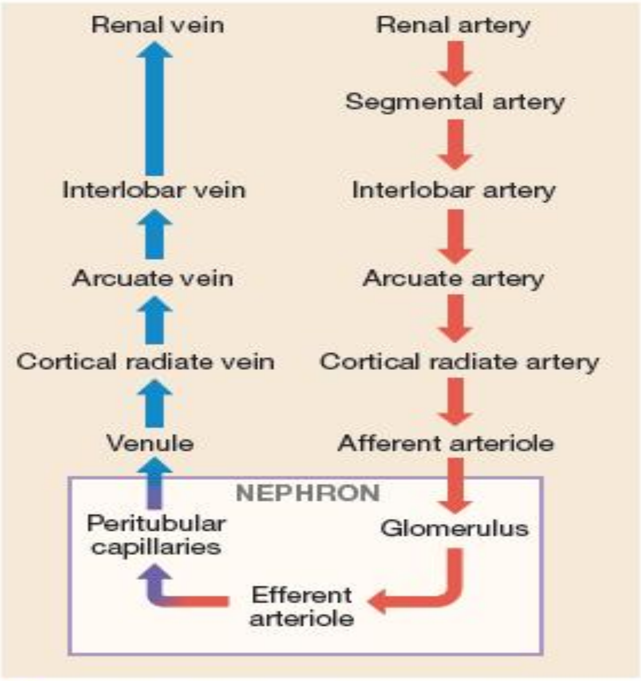
- In adult the blood flow through both kidney is 1200ml per minute.



a A sectional view, showing major arteries and veins

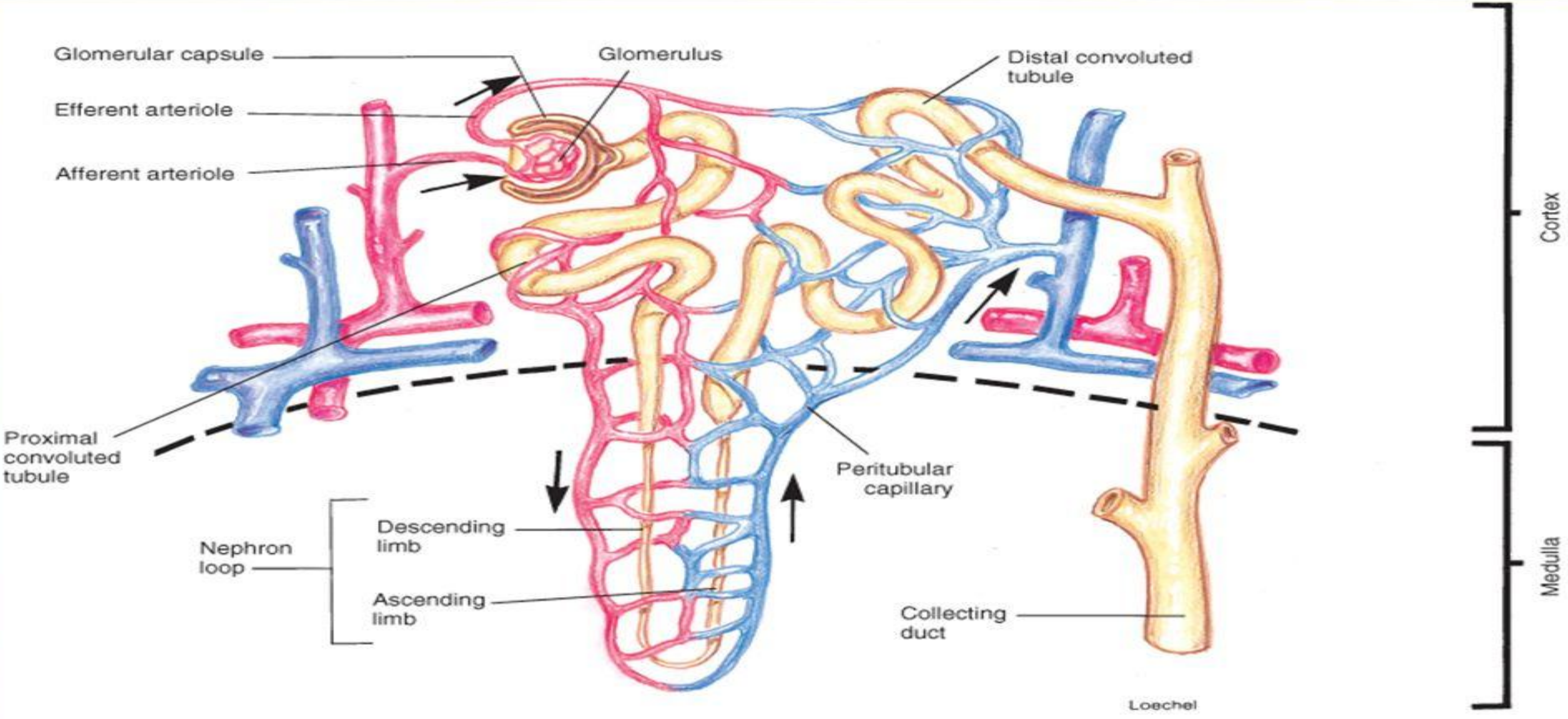


b Circulation in a single kidney lobe



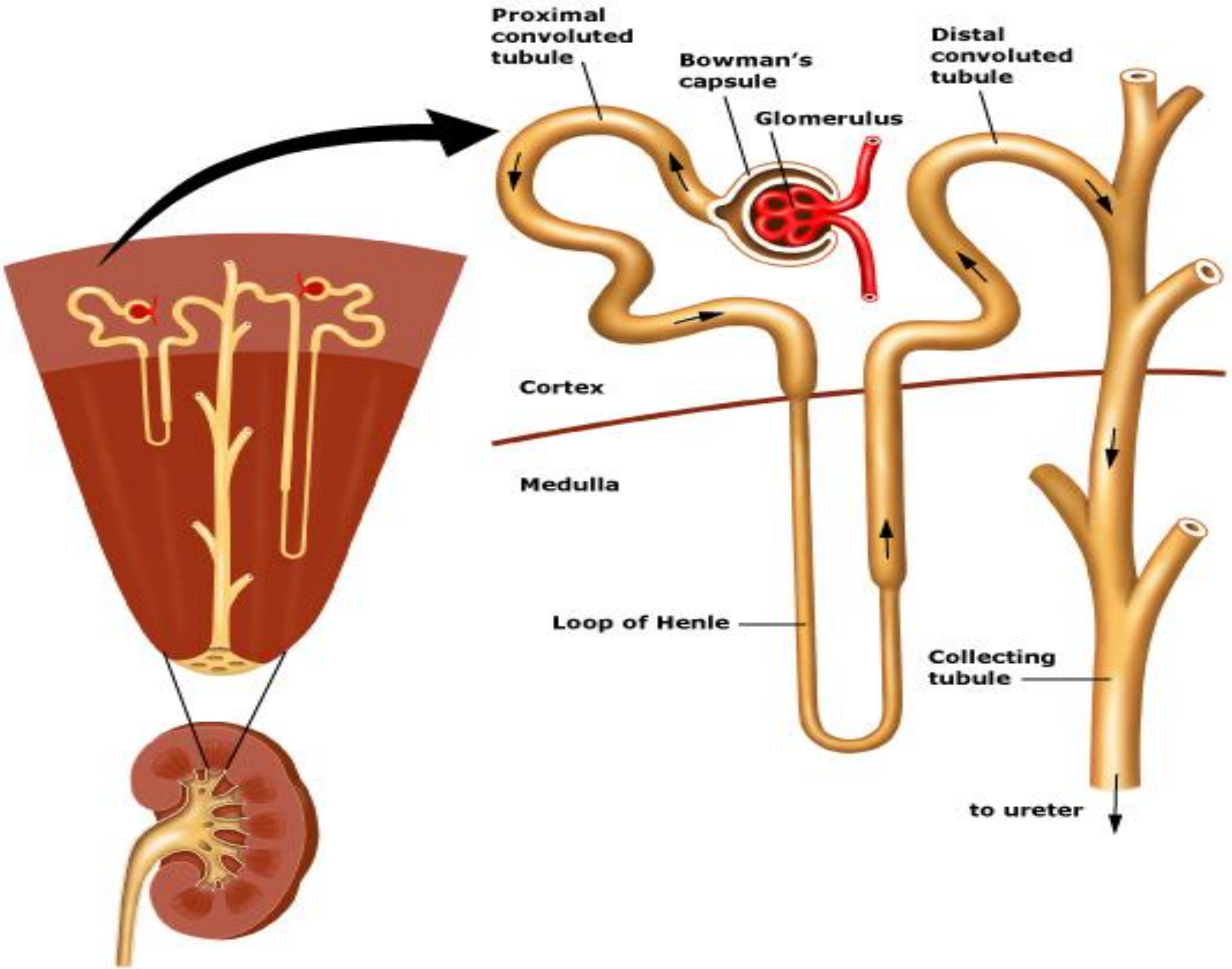
c A flowchart of renal circulation

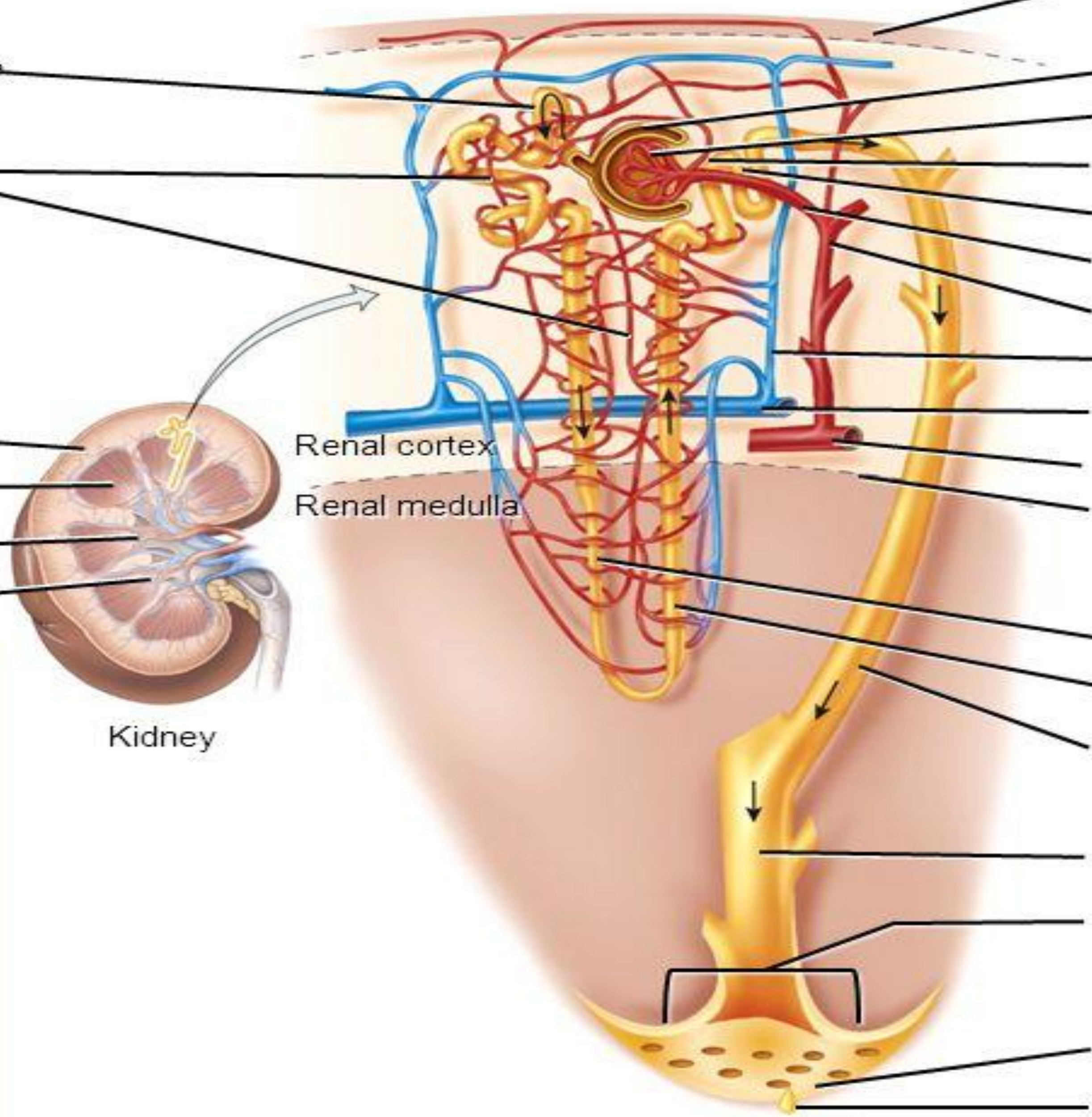
THE NEPHRON BLOOD SUPPLY



Nephron

Renal corpuscle and renal tubules



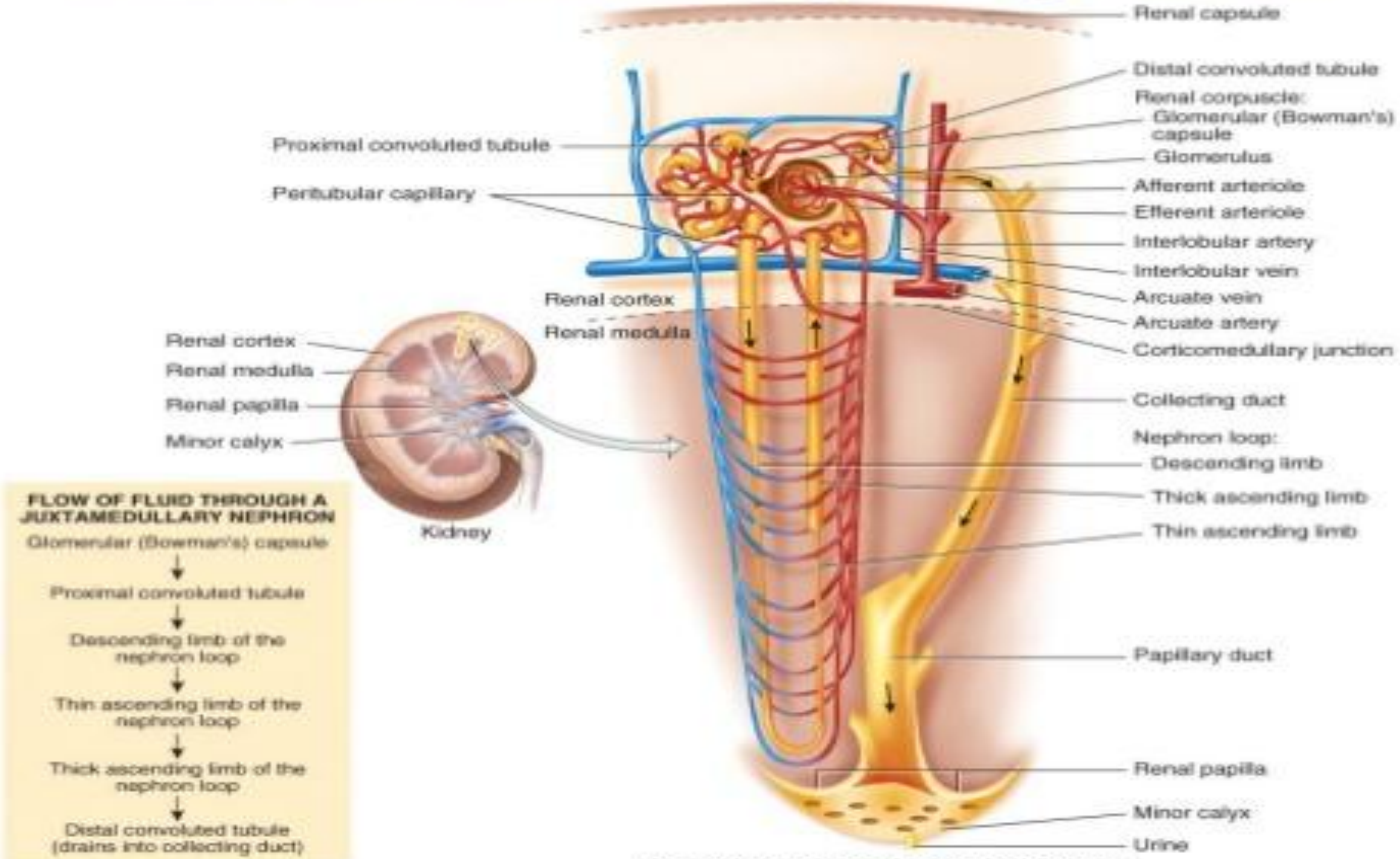


(a) Cortical nephron and vascular supply

FLOW OF FLUID THROUGH A CORTICAL NEPHRON

Glomerular (Bowman's) capsule
↓
Proximal convoluted tubule
↓
Descending limb of the loop of Henle
↓
Ascending limb of the loop of Henle
↓
Distal convoluted tubule (drains into collecting duct)

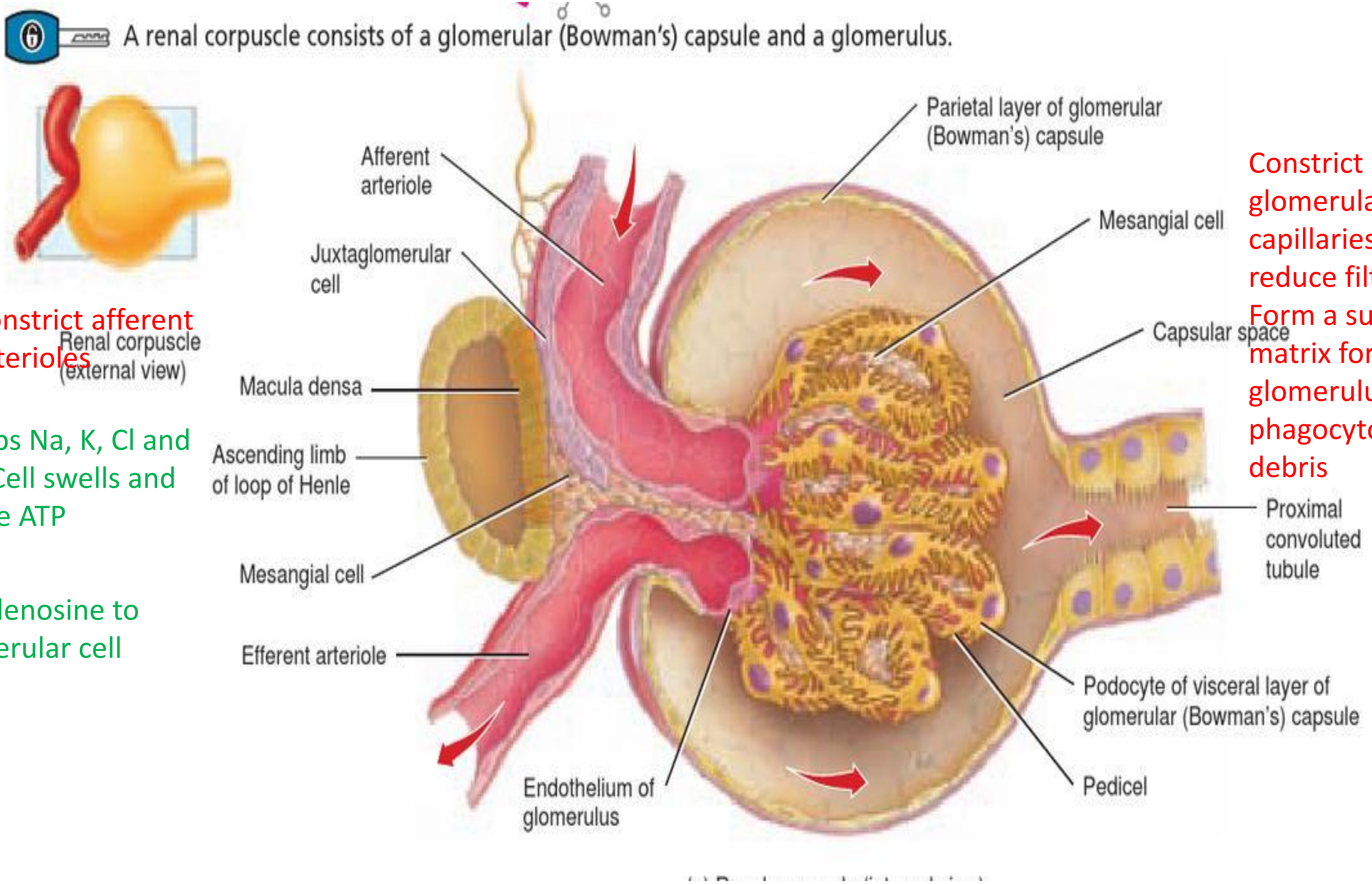
Juxtamedullary Nephron



(b) Juxtamedullary nephron and vascular supply

Lets check what you know?

- Hilum – a slit through which renal nerves, blood vessels and lymphatic system enters and ureter enters.
- 3 layers of kidney – renal fascia, perirenal fat capsule and fibrous capsule
- Renal sinus, renal papilla and renal pelvis
- Peritubular capillaries and vasa recta
- Renal corpuscle and renal tubule
- Glomerulus and glomerular capsule – 2 layers (outer simple squamous epithelial and inner podocytes, in between capsular space)



Constrict afferent arterioles

Absorbs Na, K, Cl and H2O, Cell swells and secrete ATP

Provide Adenosine to Juxtaglomerular cell

Constrict glomerular capillaries and reduce filtration. Form a supportive matrix for the glomerulus and phagocytotic tissue debris

Juxtaglomerular Apparatus

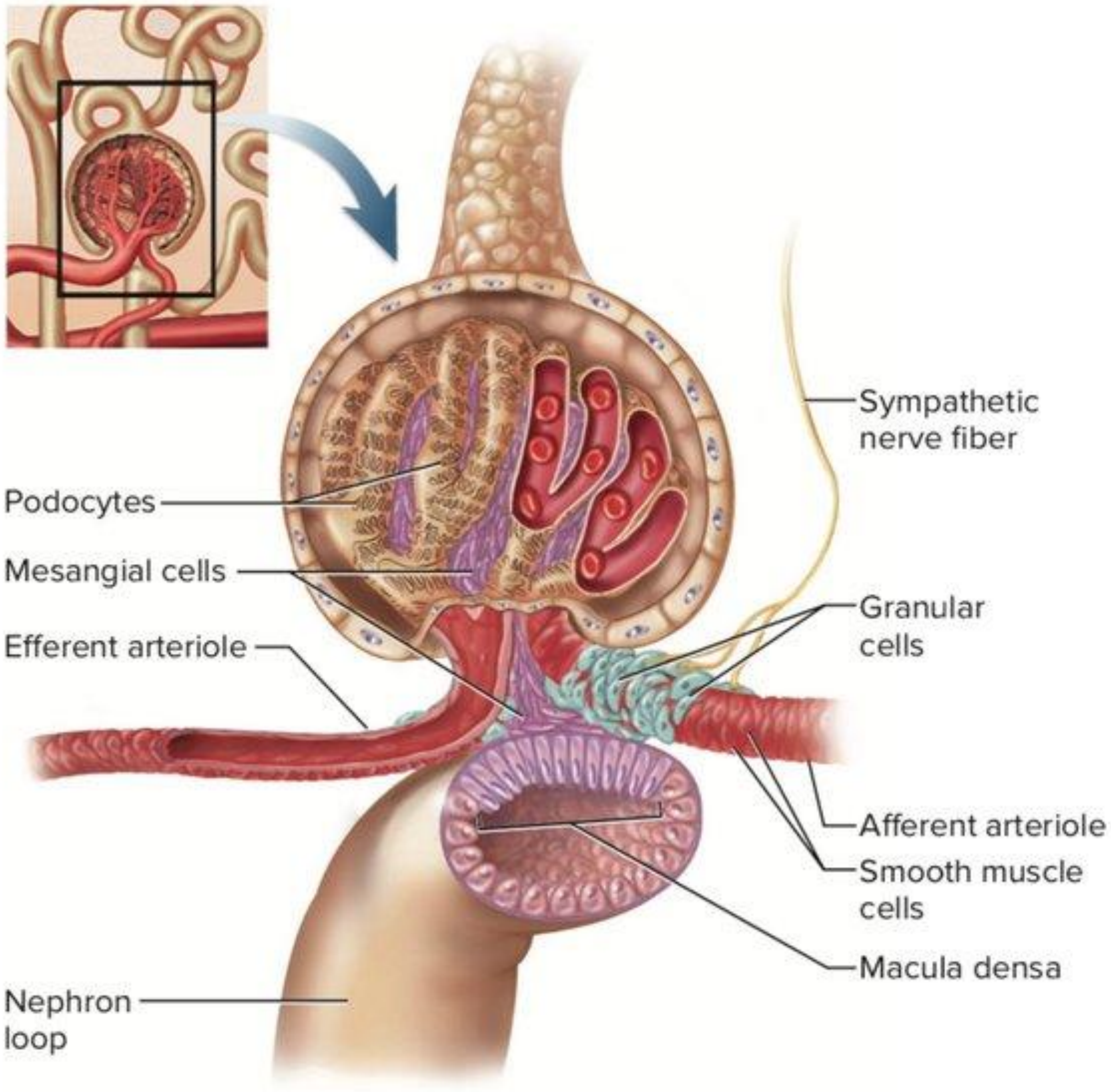
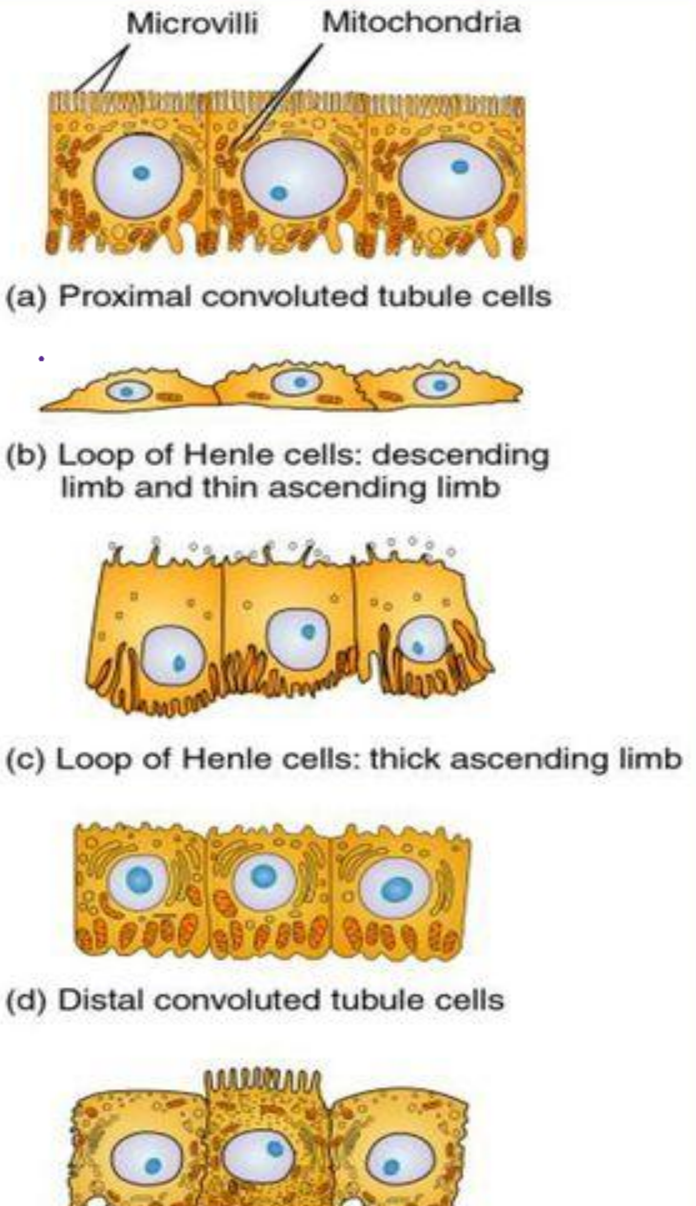


FIGURE 23.13 **The Juxtaglomerular Apparatus.**

Histology of Renal Tubule & Collecting Duct



(a) Proximal convoluted tubule cells

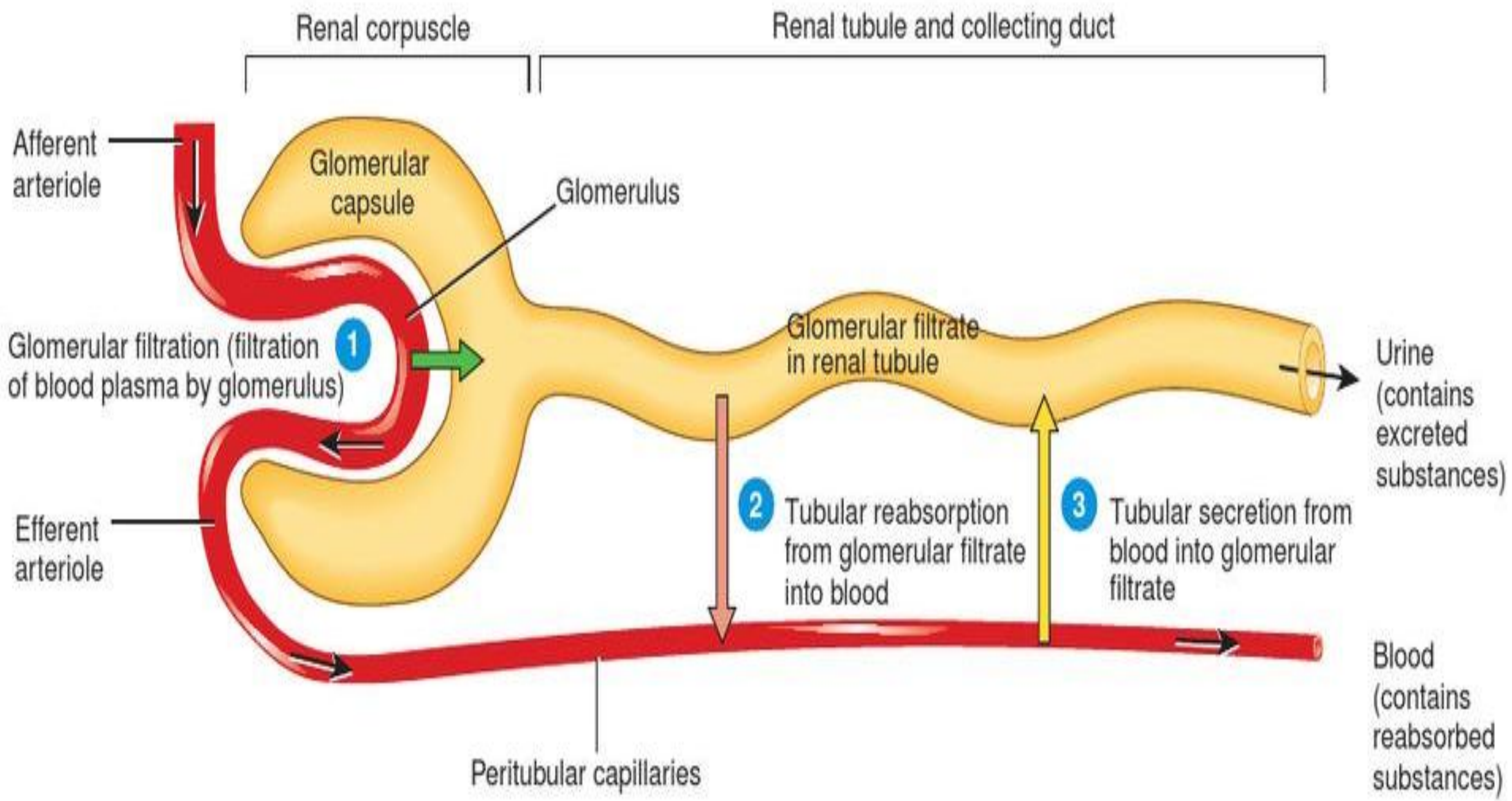
(b) Loop of Henle cells: descending limb and thin ascending limb

(c) Loop of Henle cells: thick ascending limb

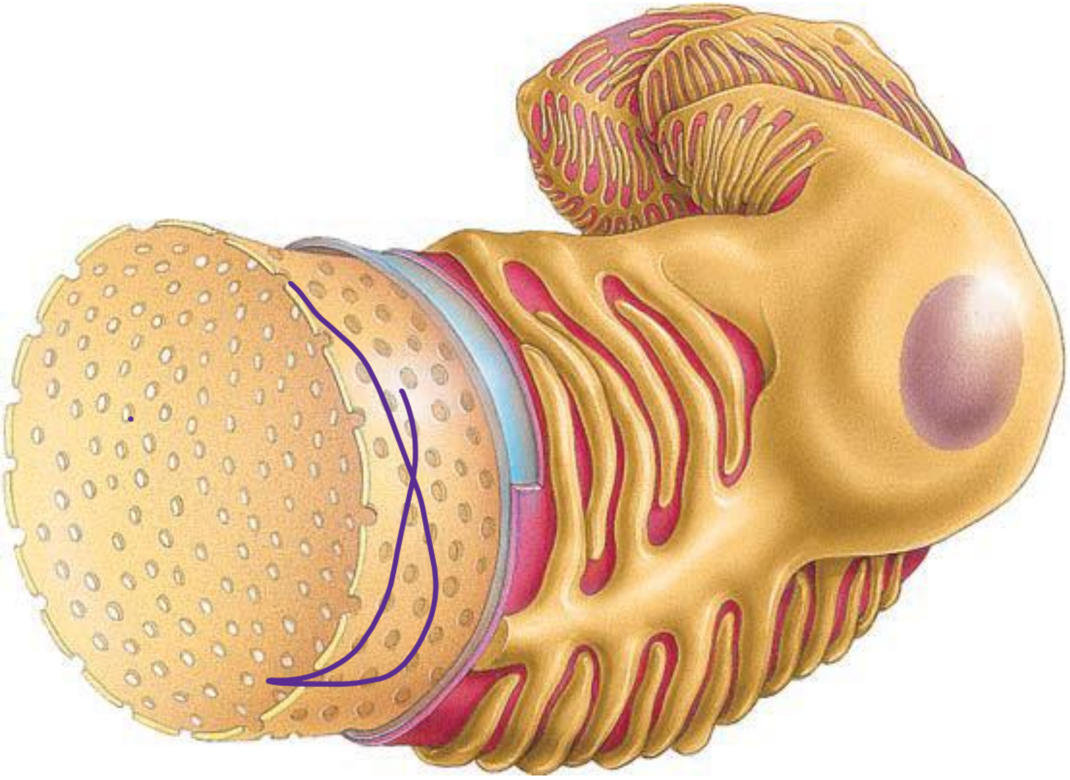
(d) Distal convoluted tubule cells

- Proximal convoluted tubule
  - simple cuboidal with brush border of microvilli that increase surface area
- Descending limb of loop of Henle
  - simple squamous
- Ascending limb of loop of Henle
  - simple cuboidal to low columnar
  - forms juxtaglomerular apparatus where makes contact with afferent arteriole
    - macula densa is special part of ascending limb
- Distal convoluted & collecting ducts
  - simple cuboidal composed of principal & intercalated cells which have microvilli

Glomerular filtration occurs in the renal corpuscle. Tubular reabsorption and tubular secretion occur all along the renal tubule and collecting duct.



Glomerular filtration



- The fluid that enters the capsular space is called the **glomerular filtrate.**
- Substances filtered from the blood cross three filtration barriers—a glomerular endothelial cell, the basal lamina, and a filtration slit formed by a podocyte.
- Glomerular endothelial cells are quite leaky because they have large **fenestrations that** measure 70–90 nm in diameter.
- The **basal lamina,** negative charges in the matrix prevent filtration of larger negatively charged plasma proteins. Exclude molecules larger than 8nm.
- Extending from each podocyte are thousands of footlike processes termed **pedicels that wrap** around glomerular capillaries. The spaces between pedicels are the **filtration slits.**
- **A thin membrane, the slit membrane,** extends across each filtration slit; it permits the passage of molecules having a diameter smaller than 3 nm, including water, glucose, vitamins, amino acids, very small plasma proteins, ammonia, urea, and ions. Most iron, calcium and thyroid hormone are bound to plasma proteins which retard their filtration by kidney.

Principle of filtration

- The use of pressure to force fluids and solutes through a membrane. However, the volume of fluid filtered by the renal corpuscle is much larger than in other capillaries of the body for three reasons:
- Glomerular capillaries present a large surface area for filtration because they are long and extensive. The mesangial cells regulate how much of this surface area is available for filtration.
- The filtration membrane is thin and porous. The thickness of the filtration membrane is only 0.1 mm. Glomerular capillaries also are about 50 times leakier than capillaries in most other tissues, mainly because of their large fenestrations.
- Glomerular capillary blood pressure is high.

Net filtration pressure

- Glomerular filtration depends on three main pressures:

1. **Glomerular blood hydrostatic pressure (GBHP) is the** blood pressure in glomerular capillaries. Generally, GBHP is about 55 mmHg. It promotes filtration by forcing water and solutes in blood plasma through the filtration membrane.
2. **Capsular hydrostatic pressure (CHP) is the hydrostatic** pressure exerted against the filtration membrane by fluid already in the capsular space and renal tubule. CHP opposes filtration and represents a “back pressure” of about 15 mmHg.
3. **Blood colloid osmotic pressure (BCOP), which is due to** the presence of proteins such as albumin, globulins, and fibrinogen in blood plasma, also opposes filtration. The average BCOP in glomerular capillaries is 30 mmHg.

Net filtration pressure (NFP) =GBHP- CHP- BCOP =10mmHg

Glomerular filtration rate

- The amount of filtrate formed in all the renal corpuscles of both kidneys each minute is the **glomerular filtration rate (GFR).**
- **In** adults, the GFR averages 125 mL/min in males and 105 mL/min in females.
- GFR is directly related to the pressures that determine net filtration pressure.
- Three mechanisms control GFR: renal autoregulation, neural regulation, and hormonal regulation.
- These mechanisms that regulate glomerular filtration rate operate in two main ways:

(1) by adjusting blood flow into and out of the glomerulus and

(2) by altering the glomerular capillary surface area available for filtration.

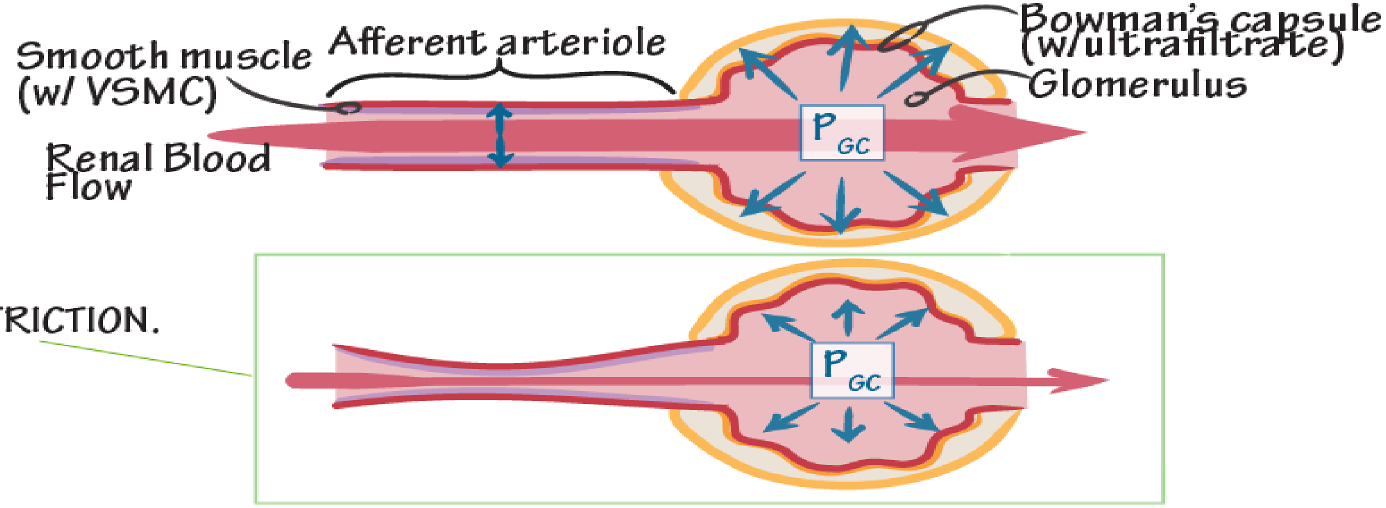
Renal Autoregulation

- The kidneys themselves help maintain a constant renal blood flow and GFR despite normal, everyday changes in blood pressure, like those that occur during exercise. This capability is called **renal autoregulation and consists of two** mechanisms—the myogenic mechanism and tubuloglomerular feedback.

Myogenic Mechanism

✓ *Relies on inherent properties of the arterioles.*

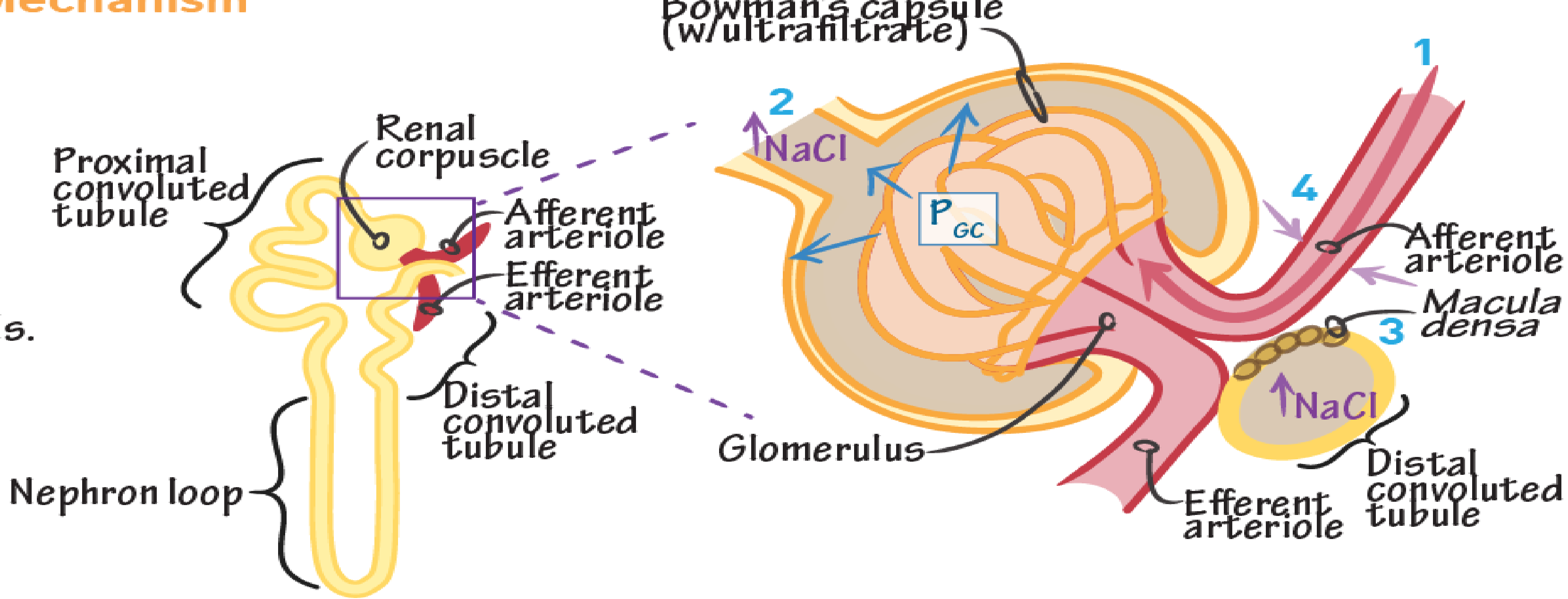
1. $\uparrow$ RBF = $\uparrow$ Hydrostatic pressure against the walls of the afferent arteriole.
2. Stretch receptors in VSMC initiate VASOCONSTRICTION.
3. $\downarrow$ RBF = $\downarrow P_{GC}$ = $\downarrow$ GFR



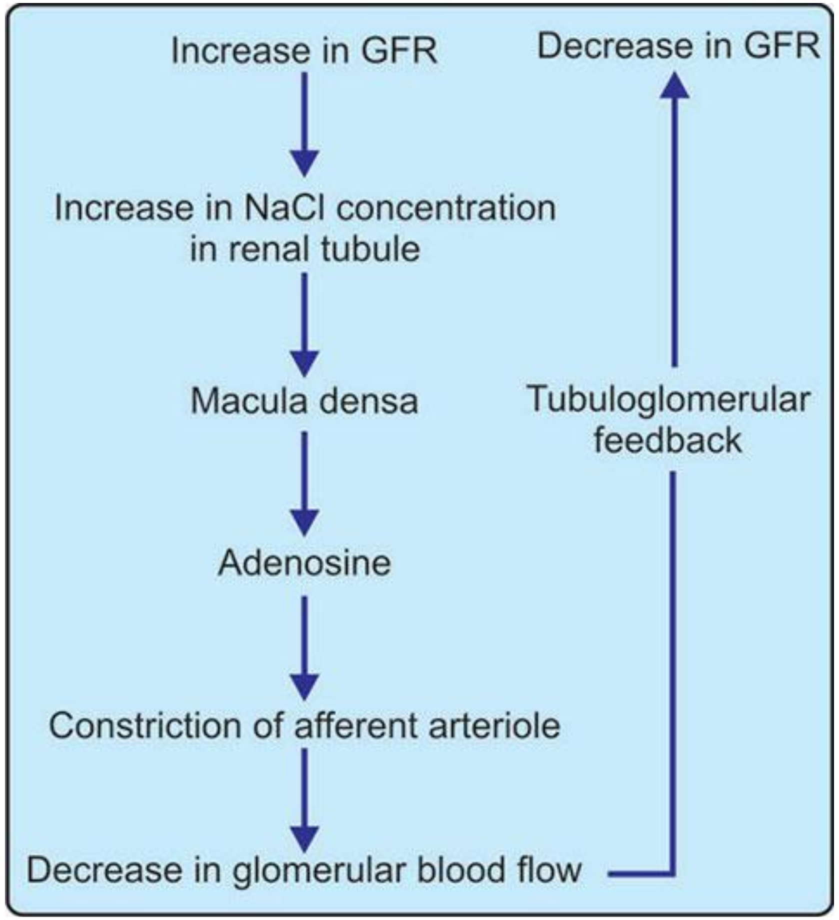
Tubuloglomerular Feedback Mechanism

✓ *Relies on interaction between the nephron tubule and glomerulus.*

1. $\uparrow$ RBF = $\uparrow P_{GC}$ = $\uparrow$ GFR
2. $\uparrow$ GFR = $\uparrow$ Salt in ultrafiltrate
3. Macula densa senses $\uparrow$ salt, releases vasoconstrictor chemicals.
4. Afferent arteriole constricts.
5. $\downarrow$ RBF = $\downarrow P_{GC}$ = $\downarrow$ GFR



Tubuloglomerular feedback.



Hormonal autoregulation

- Two hormones contribute to regulation of GFR. Angiotensin II reduces GFR; atrial natriuretic peptide (ANP) increases GFR.
- **Angiotensin II is a very potent vasoconstrictor** that narrows both afferent and efferent arterioles and reduces renal blood flow, thereby decreasing GFR.
- Cells in the atria of the heart secrete **atrial natriuretic peptide (ANP).** Stretching of the atria, as occurs when blood volume increases, stimulates secretion of ANP. By causing relaxation of the glomerular mesangial cells, ANP increases the capillary surface area available for filtration. Glomerular filtration rate rises as thesurface area increases.

Neural Regulation

- Blood vessels of the kidneys are supplied by sympathetic ANS fibers that release norepinephrine. Norepinephrine causes vasoconstriction through the activation of 1 receptors, which are particularly plentiful in the smooth muscle fibers of afferent arterioles.
- During mild constriction : blood flow in and out are constricted by same level.
- During high constriction : Afferent get more stimulated and reduce GFR.

Tubular reabsorption and tubular secretion

Substance	Filtered* (Enters Glomerular Capsule per Day)	Reabsorbed (Returned to Blood per Day)	Urine (Excreted per Day)
Water	180 liters	178–179 liters	1–2 liters
Proteins	2.0 g	1.9 g	0.1 g
Sodium ions (Na^+)	579 g	575 g	4 g
Chloride ions (Cl^-)	640 g	633.7 g	6.3 g
Bicarbonate ions (HCO_3^-)	275 g	274.97 g	0.03 g
Glucose	162 g	162 g	0 g
Urea	54 g	24 g	30 g†
Potassium ions (K^+)	29.6 g	29.6 g	2.0 g‡
Uric acid	8.5 g	7.7 g	0.8 g
Creatinine	1.6 g	0 g	1.6 g

Secreted substances include hydrogen ions (H), K, ammonium ions (NH4), creatinine, and certain drugs such as penicillin. Tubular secretion has two important outcomes: (1) The secretion of H helps control blood pH. (2) The secretion of other substances helps eliminate them from the body.

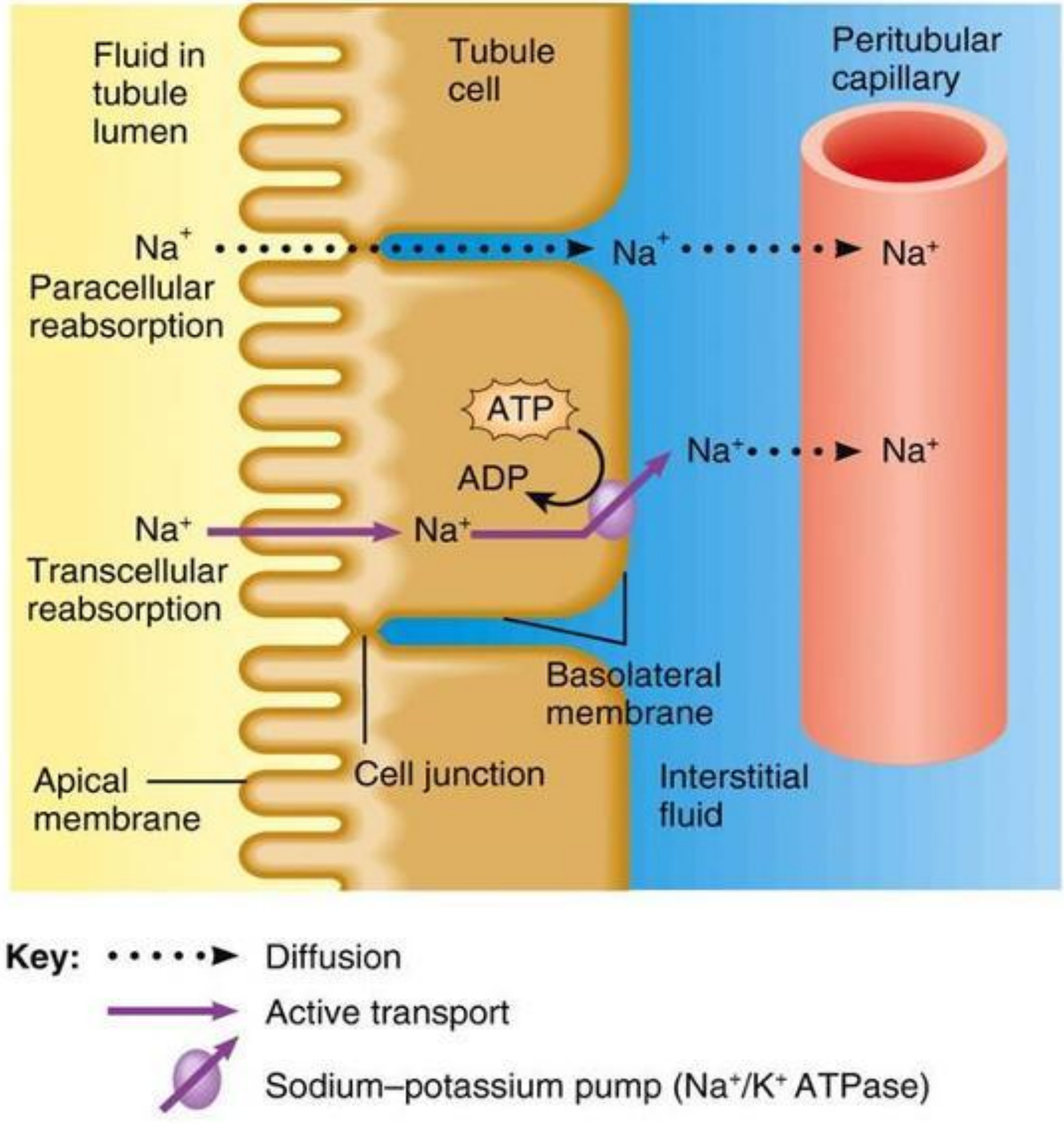
Reabsorption routes

Fluid can leak *between the cells in a passive process known as* **paracellular reabsorption .**

Even though the epithelial cells are connected by tight junctions, the tight junctions between cells in the proximal convoluted tubules are “leaky” and permit some reabsorbed substances to pass between cells into peritubular capillaries.

In some parts of the renal tubule, the paracellular route is thought to account for up to 50% of the reabsorption of certain ions and the water that accompanies them via osmosis.

Transcellular- from cell to interstitial fluid and then to capillary.



Transport mechanism across the tube

Transport Mechanisms Across the Tubule

Active Transport

- Requires energy.
- Moves substances against their electrochemical gradient.

Primary active

Directly coupled to energy source.

e.g. Na+-K+ ATPase.

Secondary active

Indirectly coupled to energy source.

Carrier protein.

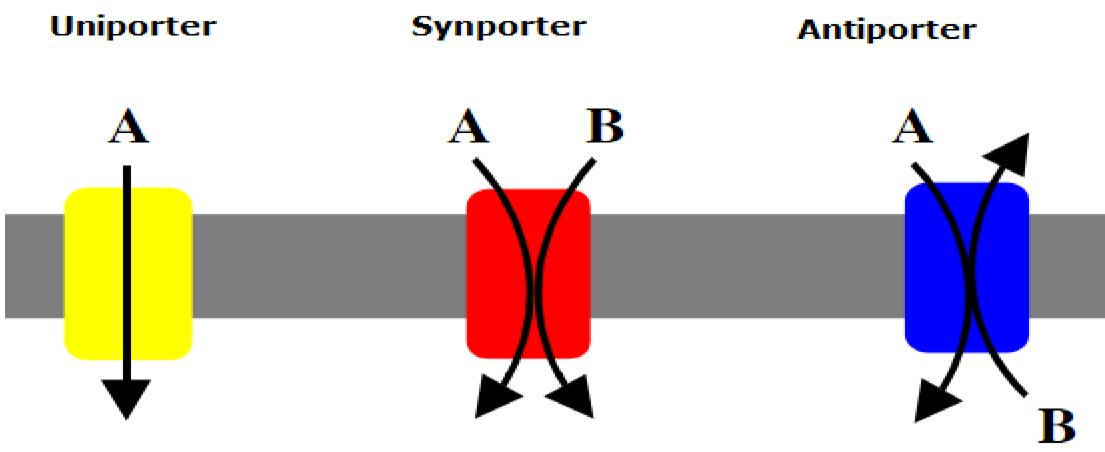
e.g. Glucose & a.a.

Passive Transport

- Does not need energy.
- Moves substances down their electrochemical gradient.

Passive diffusion
Osmosis

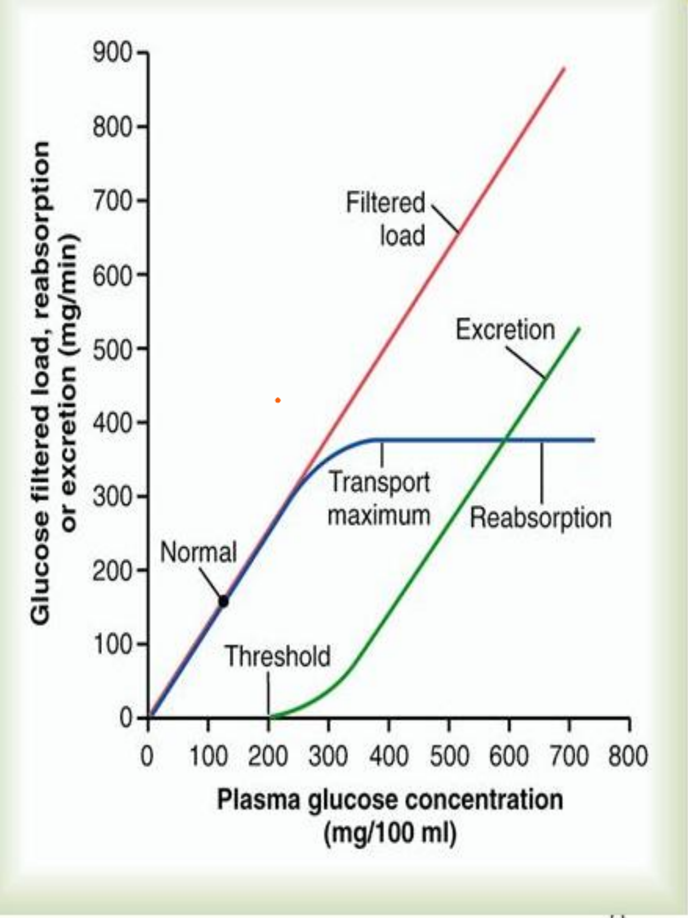
Water
Solutes like Cl-
Urea



Transport mechanism

Transport maxima Tm- the rate at which the substance is reabsorbed in the renal tubule. The rate of reabsorption of any substance depends upon the rate at which specific transport system works. This transport system depends upon the carrier substance or enzymes. For glucose 300 to 375mg/minute.

Renal threshold of any substances- Below this level the substance is completely reabsorbed and does not appear in urine. E,g. for glucose- 180mg/dL



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- Threshold substances
  - High threshold substances –never appear in urine, e.g, glucose, amino acid, acetoacetate ions and vitamins
  - Low threshold substances- appear in urine even under normal condition- urea, uric acid and phosphates
  - Non-threshold substance- substances which are not at all reabsorbed and excreted in urine- creatinine

SODIUM REABSORPTION: PROXIMAL TUBULE

Sodium Balance

SODIUM INTAKE = SODIUM EXCRETION

SODIUM IS THE MAJOR CATION OF THE ECF; ITS AMOUNT DETERMINES ECF VOLUME, PLASMA VOLUME, BLOOD VOLUME, AND BLOOD PRESSURE.

TWO-THIRDS (67%) OF SODIUM REABSORPTION OCCURS IN PROXIMAL TUBULE.

REABSORPTION IS COUPLED WITH REABSORPTION OF OTHER SOLUTES AND WATER.

Glomerulotubular Balance

MAINTAINS NEARLY CONSTANT RATE OF SODIUM REABSORPTION DESPITE CHANGES IN GFR.

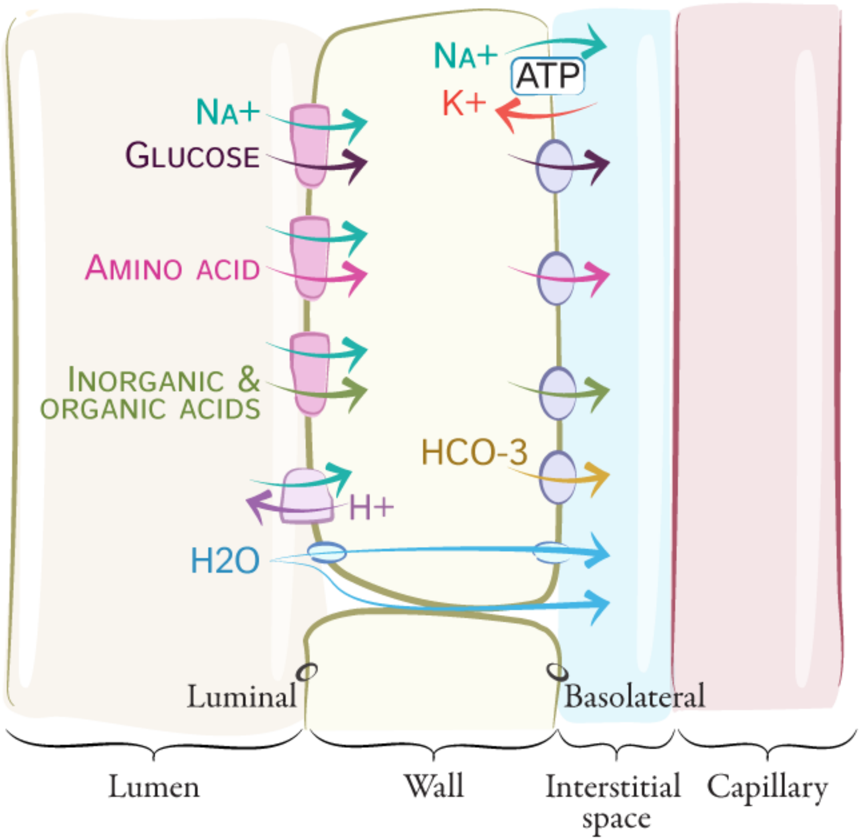
IN RESPONSE TO CHANGES IN GFR, PROXIMAL TUBULE ALTERS TOTAL AMOUNT OF SODIUM REABSORBED SO THAT THE RATE OF SODIUM REABSORPTION IS HELD AT 67%.

GLOMERULOTUBULAR BALANCE CAN CHANGE IN REPONSE TO CHANGES IN ECF VOLUME:

- ECF VOLUME CONTRACTS, REABSORPTION OF SODIUM AND WATER INCREASES TO INCREASE ECF VOLUME.
- ECF VOLUME EXPANDS, REABSORPTION DECREASES TO REDUCE ECF VOLUME.

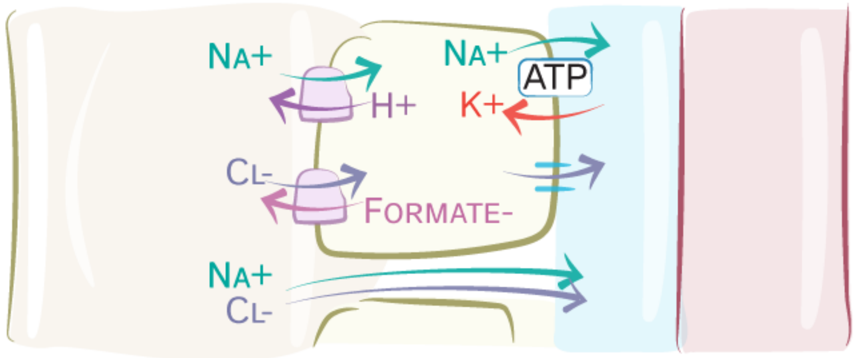
Early Proximal Tubule

Na^+ reabsorp. is linked to Nutrients, Acids, H^+ secretion

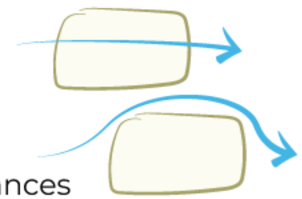


Late Proximal Tubule

Na^+ reabsorp. is linked to Cl^-



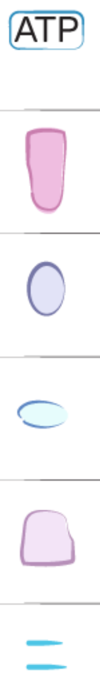
Pathways



TRANSCELLULAR pathway transports substances through tubule cells.

PARACELLULAR pathway moves substances through "leaky" tight junctions between tubule cells.

Mechanisms



ATP	**Na+-K+ ATPase** — Moves Na+ out of the cell and K+ into cell; Creates electrochemical gradient.
	Cotransporters — Transport solutes in same direction.
	Facilitated diffusion — Protein carriers or channels regulate diffusion.
	AQP1 — Water channels.
	Counter transporters — Transport solutes in opposite directions.
	Simple diffusion — Solutes move down electrochemical gradient.

SODIUM REABSORPTION: DISTAL NEPHRON

Sodium Balance

Sodium intake = Sodium excretion

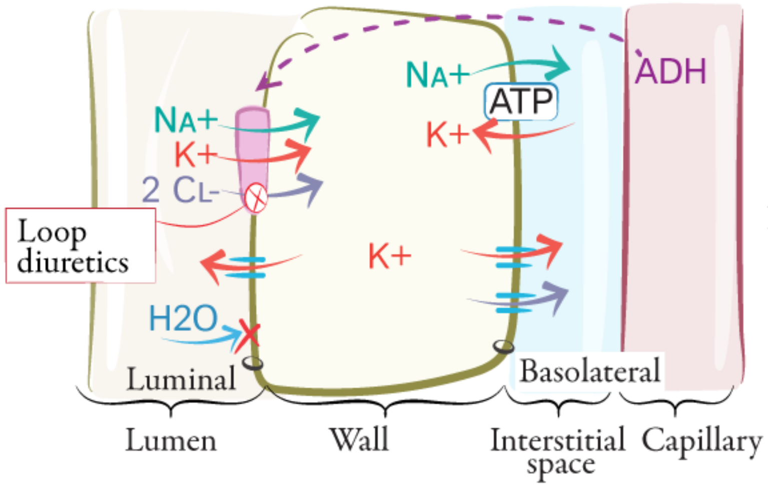
Less than 1% of filtered load is excreted in urine.

Na+ reabsorption is load-dependent in distal segments.

Reabsorption rate remains constant despite changes in filtered load.

Thick Ascending Limb: 25%

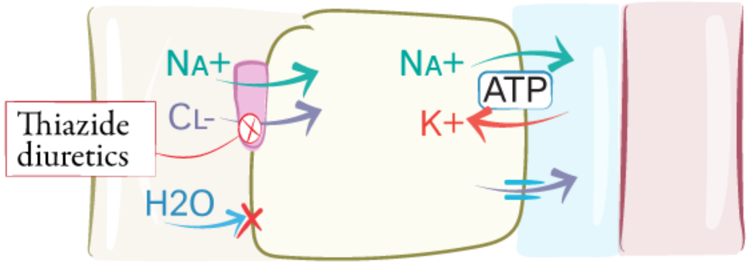
- Na+, K+, and Cl- reabsorption linked.



Diluting segment;
No water reabsorbed.

Early Distal Tubule: 5%

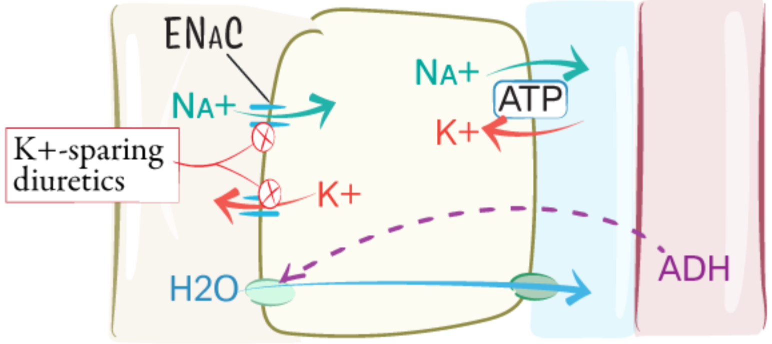
- Na+ and Cl- reabsorption are linked.



Cortical diluting segment;
No water reabsorbed.

Late Distal Tubule & Collecting Duct: 3%

- Na+ reabsorption is linked to K+ secretion in principal cells.



Aldosterone increases reabsorption of Na+ and K+ secretion.

ADH required for H2O to be reabsorbed.

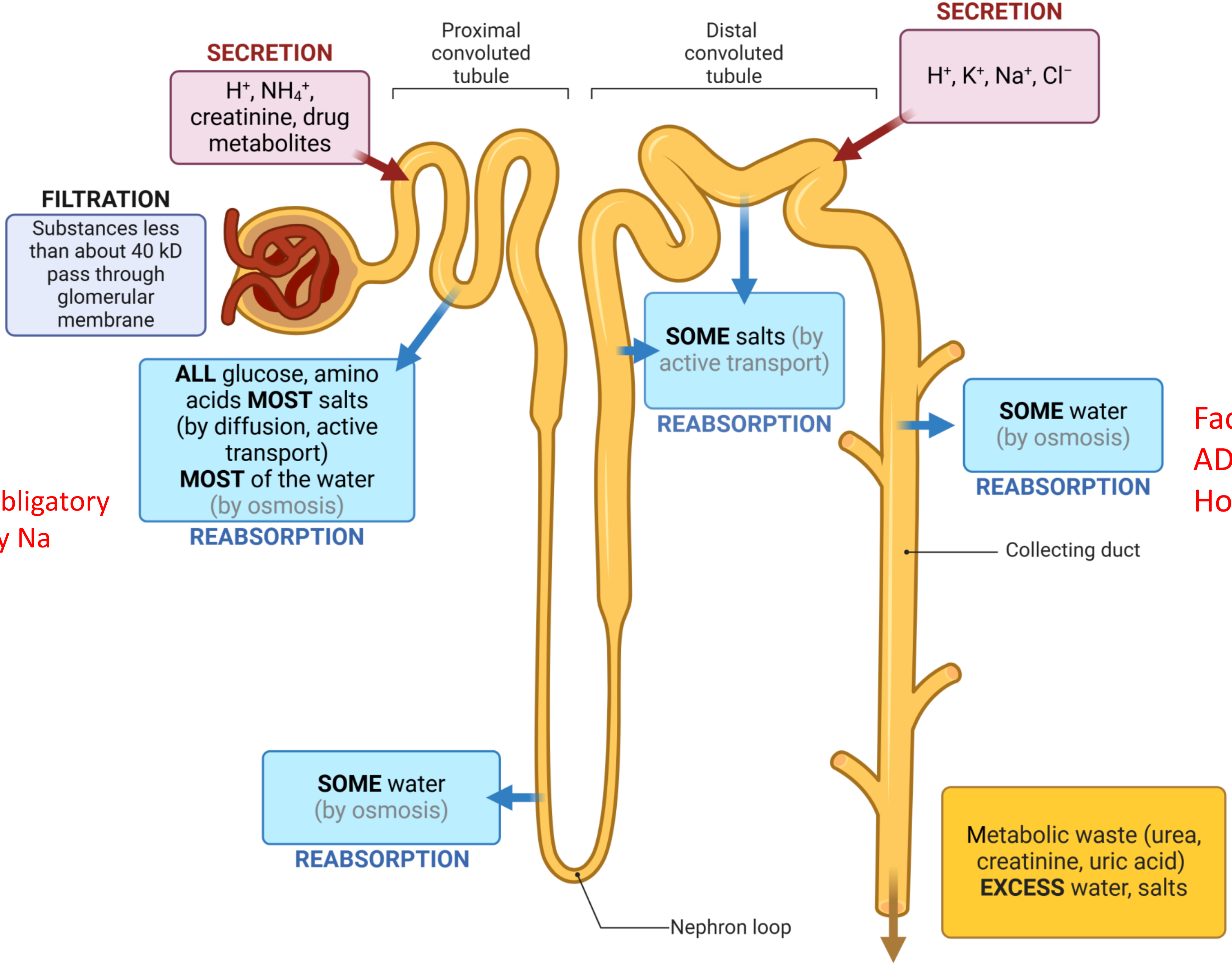
Mechanisms	
ATP	Na+-K+ ATPase — Moves Na+ out of the cell & K+ into cell; Creates electrochemical gradient.
	Cotransporters — Transport solutes in same direction.
	Simple diffusion — Solutes move down electrochemical gradient.
	AQP2 — Luminal water channels.
	AQP3 & 4 — Basolateral water channels.

Sodium-Blocking Diuretics

Loop diuretics — Block Cl- binding site on Na+- K+-Cl- cotransporter.

Thiazide diuretics — Block Cl- binding site on Na+- Cl- cotransporter.

K+ - sparing diuretics — Reduce Na+ reabsorption and K+ secretion.

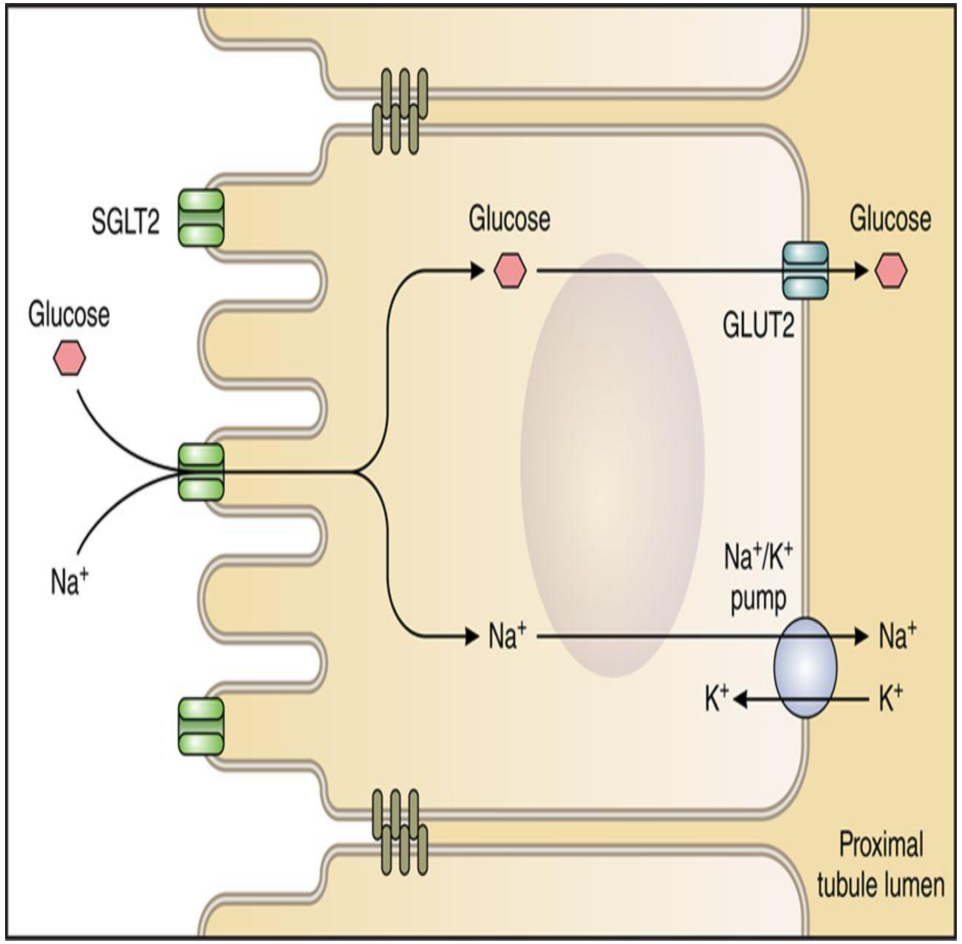


Obligatory by Na

Facultative by ADH-Anti Diuretic Hormone

Reabsorption in PCT and DLOH

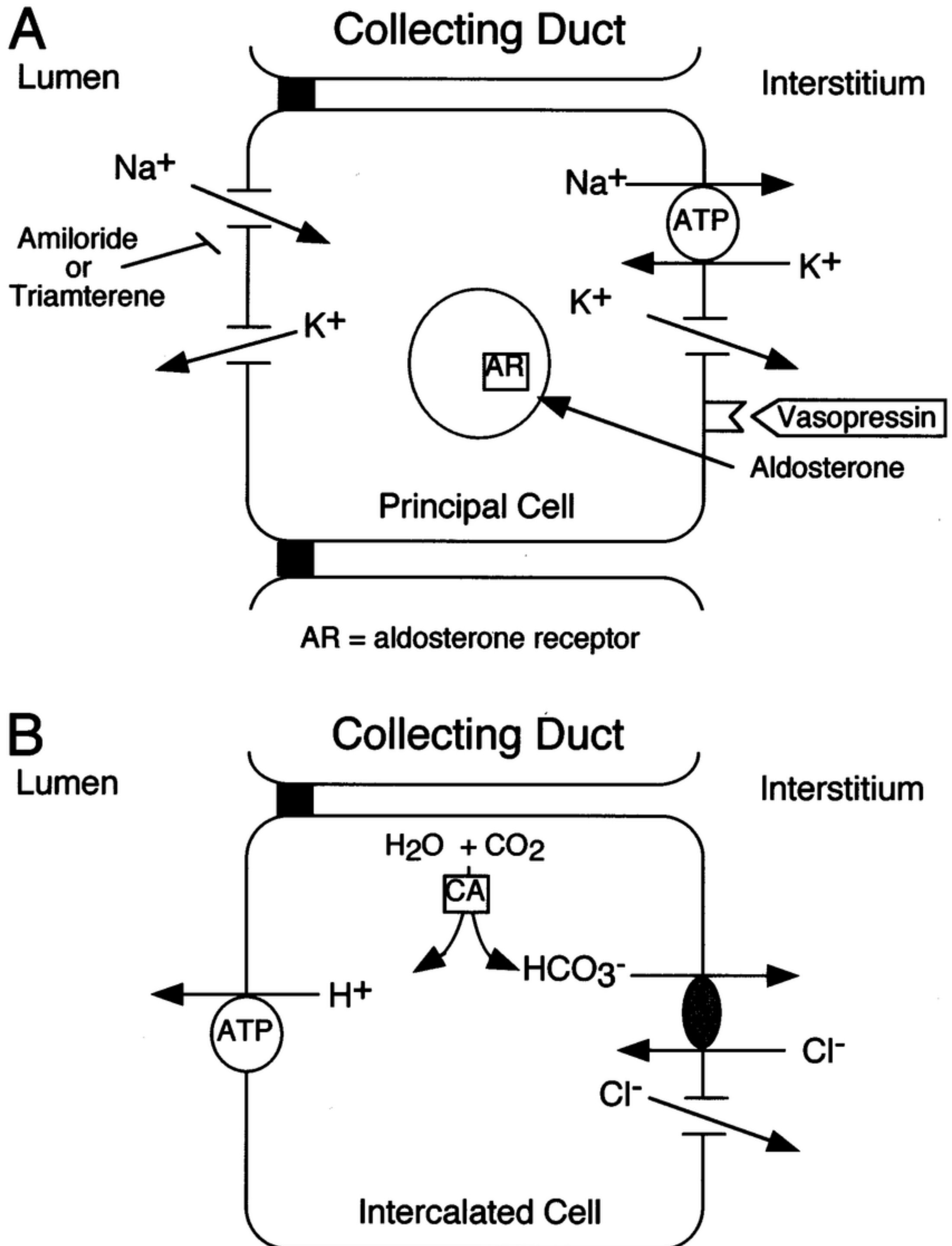
- The largest amount of solute and water reabsorption from filtered fluid occurs in the proximal convoluted tubules, which reabsorb 65% of the filtered water, Na, and K; 100% of most filtered organic solutes such as glucose and amino acids; 50% of the filtered Cl; 80–90% of the filtered HCO3 ; 50% of the filtered urea; and a variable amount of the filtered Ca2, Mg2, and HPO4 2 (phosphate).
- In addition, proximal convoluted tubules secrete a variable amount of H ions, ammonium ions (NH4), and urea.
- Most solute reabsorption in the proximal convoluted tubule (PCT) involves Na.
- Na symporters in the PCT reclaim filtered HPO4 2 (phosphate) and SO4 2 (sulfate) ions, all amino acids, and lactic acid in a similar way.
- Solute reabsorption in proximal convoluted tubules promotes osmosis of water.
- In other words, reabsorption of the solutes creates an osmotic gradient that promotes the reabsorption of water via osmosis. They carry aquaporins.



Uptake by the Peritubular capillaries

- The mechanism of capillary absorption are osmosis and solvent drag.
- Three factors promote osmosis:
  - The accumulation of reabsorbed fluid on the basal side of the epithelium cells create a high tissue fluid pressure that physically drives water into the capillaries.
  - The narrowness of the efferent arteriole lowers the blood hydrostatic pressure from 60mmHg in glomerulus to only 8 mmHg in the peritubular capillaries.
  - As blood passes through the glomerulus, a lot of water is filtered and elevate the colloidal osmotic pressure.

DCT


A
Collecting Duct
Lumen
Interstitium
Na+
Amiloride
or
Triamterene
K+
Na+
ATP
K+
K+
AR
Vasopressin
Aldosterone
Principal Cell
AR = aldosterone receptor
B
Collecting Duct
Lumen
Interstitium
H2O + CO2
CA
HCO3-
H+
ATP
Cl-
Cl-
Intercalated Cell

Secretion

- Penicillin
- Amino derivatives
- Diodrast
- PAH- para-aminohippuric acid

- https://www.google.com/search?sca_esv=53017b0e41c9f5f0&rlz=1C1VDKB_en-GBIN1107IN1107&sxsrf=ADLYWIL_wyADrUkarN9c009iTZ75ieciSA:1729057201265&q=uptake+by+peritubular+capillaries&tbm=vid&source=lnms&fbs=AEQNm0CvspUPonaF8UH5s_LBD3JPX4RSeMPt9v8oIaeGMh2T2PRrsfVPlQRxSTpQ4UUI6wfsFlEVaMALnJjEZtYpSTLmUV5oGF4fnHSG0LbvLjVKUV0IWX-9yHknaXpsINbxRPK_rD0aGBXyqo-cUa2T6ZySNg4d875n-vXkSutq7bWvEyjXRQuBfWktFSUkoyoeiqhKHNE-BZiSEnsk93CG_Dl8i5jDTw&sa=X&ved=2ahUKEwjug5yCmJKJAxUvTmwGHZ8_LJoQ0pQJegQIDhAB&biw=1536&bih=730&dpr=1.25#fpstate=ive&vld=cid:4a660109,vid:yQORERbBEq0,st:0