Renal Physiology

Eastern and Greater Southern Surgical Skills Network - GSSE Education

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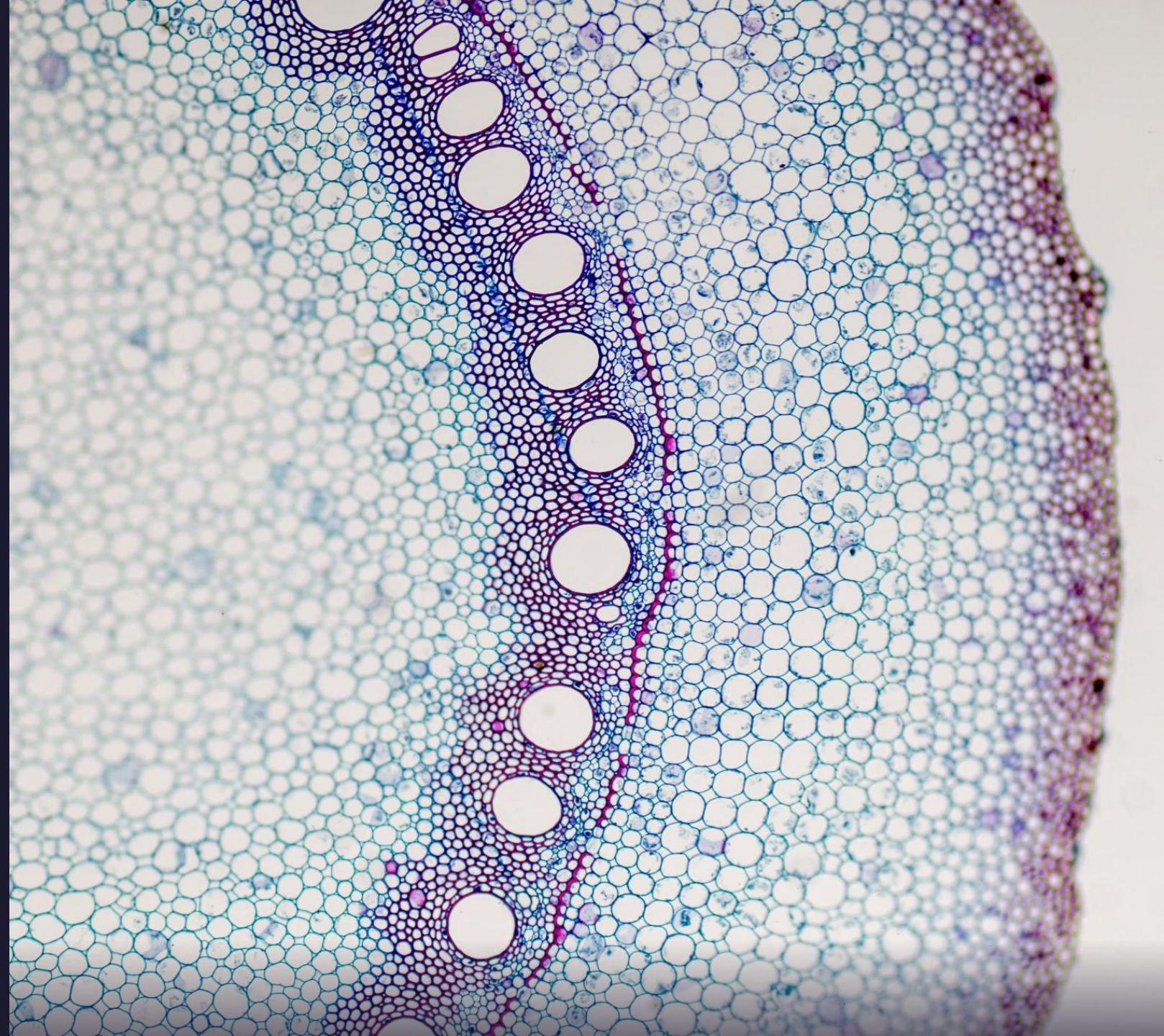
5/4/21



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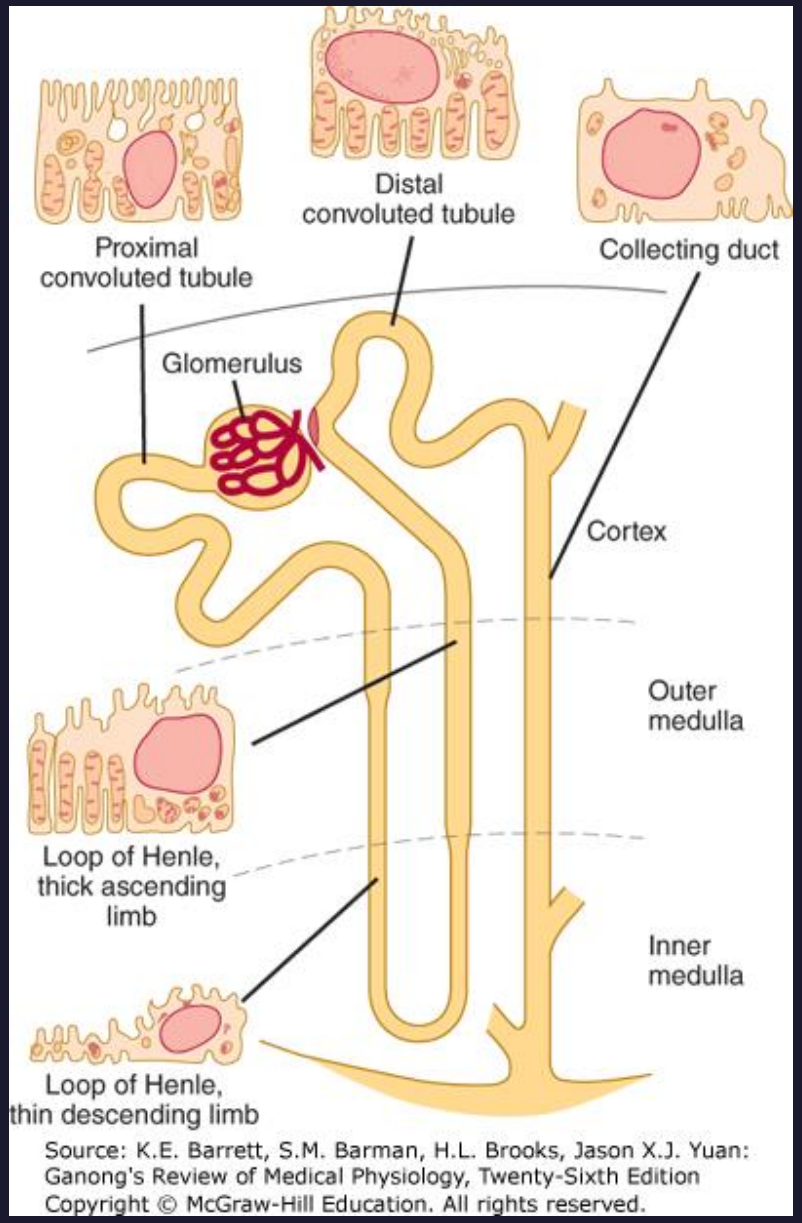
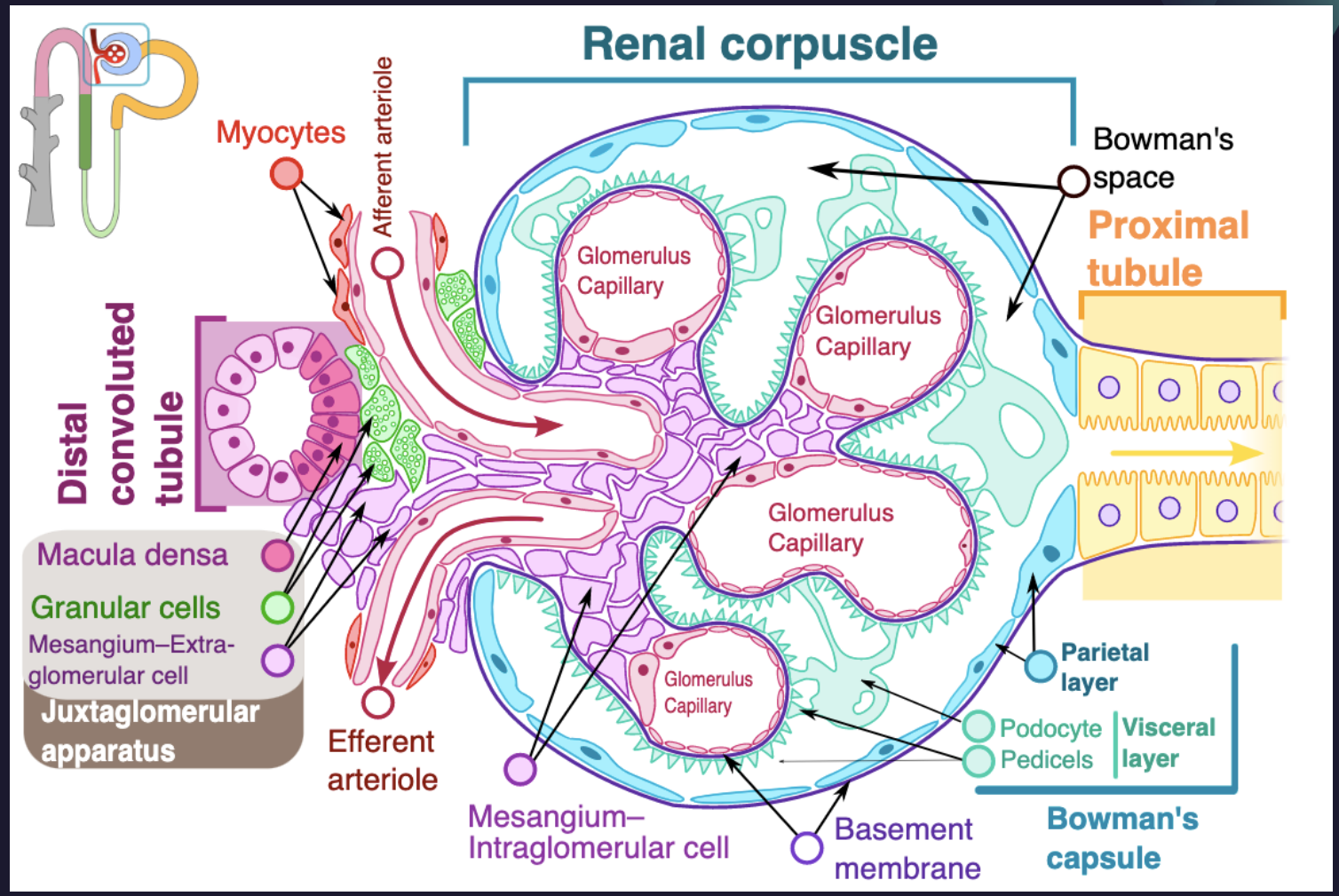


GSSE tips

- Have a good understanding of basic key principles
- Videos, diagrams: Youtube: Armando Hasudungan’s Nephrology series, https://teachmephysiology.com
- Supplement with detail from reference material: Ganongs, Leon Lai’s Notes
- Once material learnt, test yourself as much as possible!!!

The Glomerulus

- Blood flows in via the afferent arterioles
- Blood flows through the glomerulus capillaries and filtrate passes through the basement membrane into the Bowman's Space
- Filtrate passes into the proximal tubule
- The remaining blood flows through the efferent arterioles



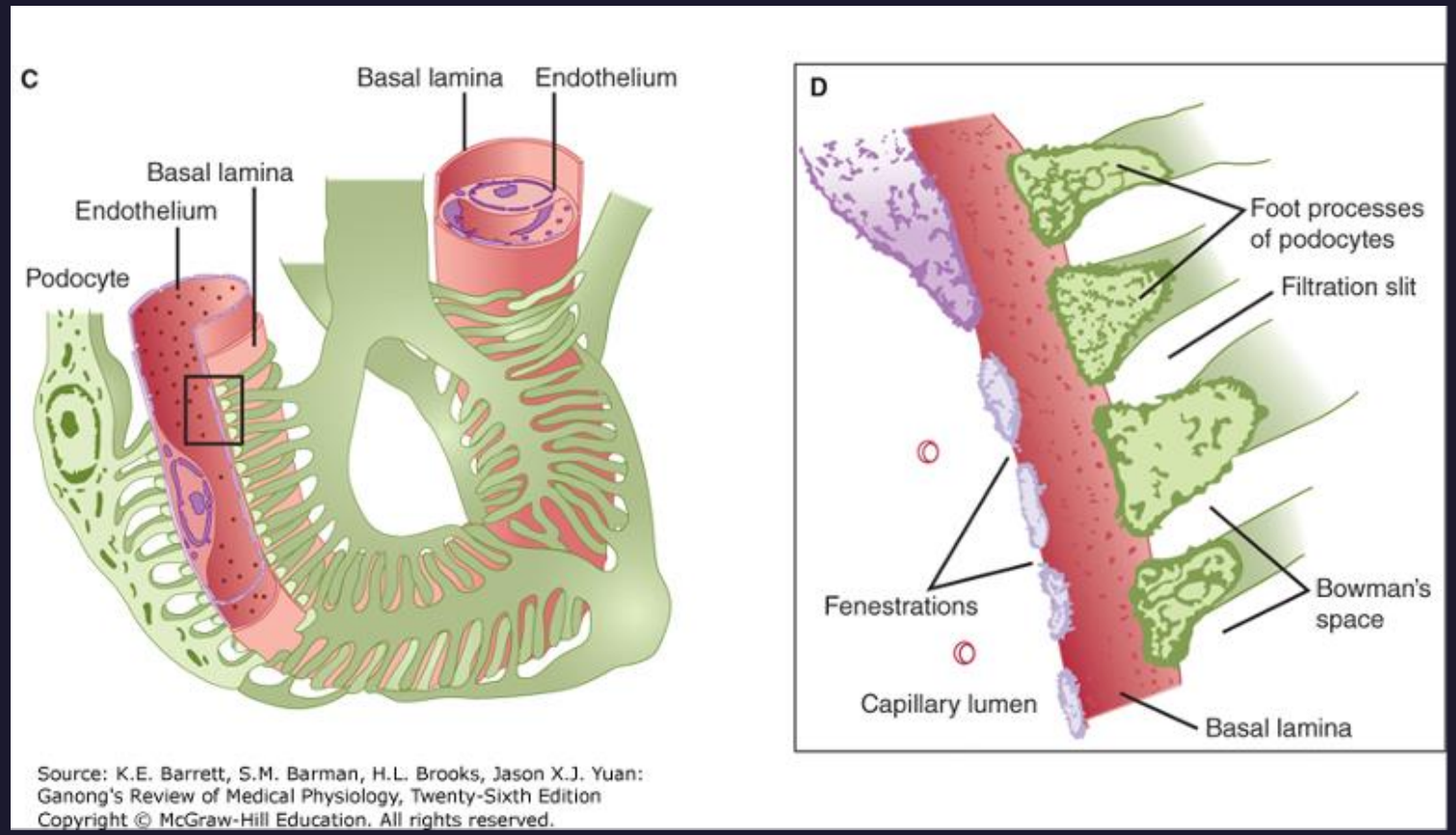
Glomerular Filtration 1

- Fluid – Controlled by glomerular filtration pressures
- Solutes – Difficult for large or positively charged molecules to filter into Bowman's Space

1. Filtration Slits – Limit large molecules (proteins) 8nm
2. Proteoglycans in the BM and Foot processes – Create a negative charge

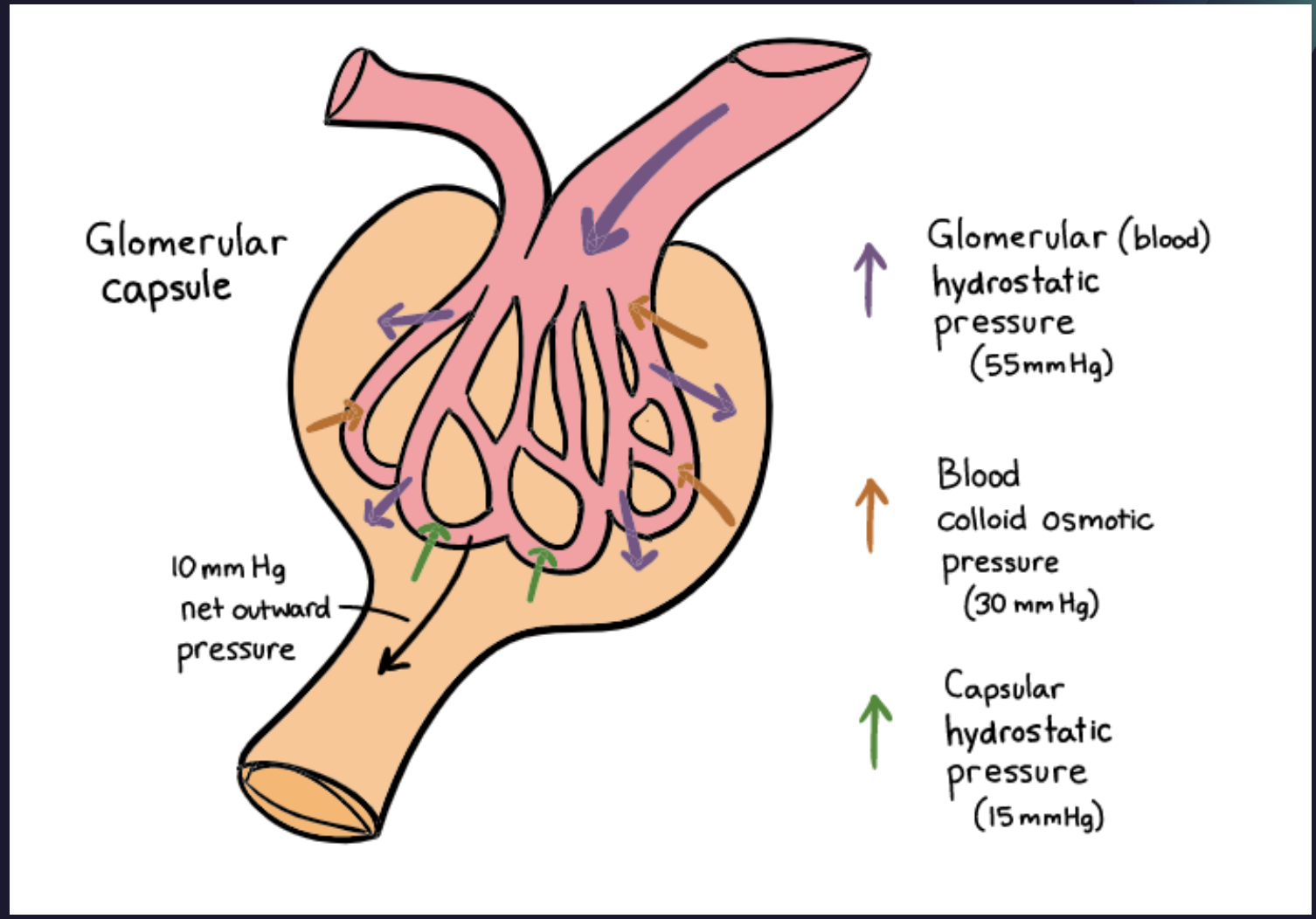
PASS: K+, Na+, Cl-

DO NOT PASS: Proteins, incl. albumin



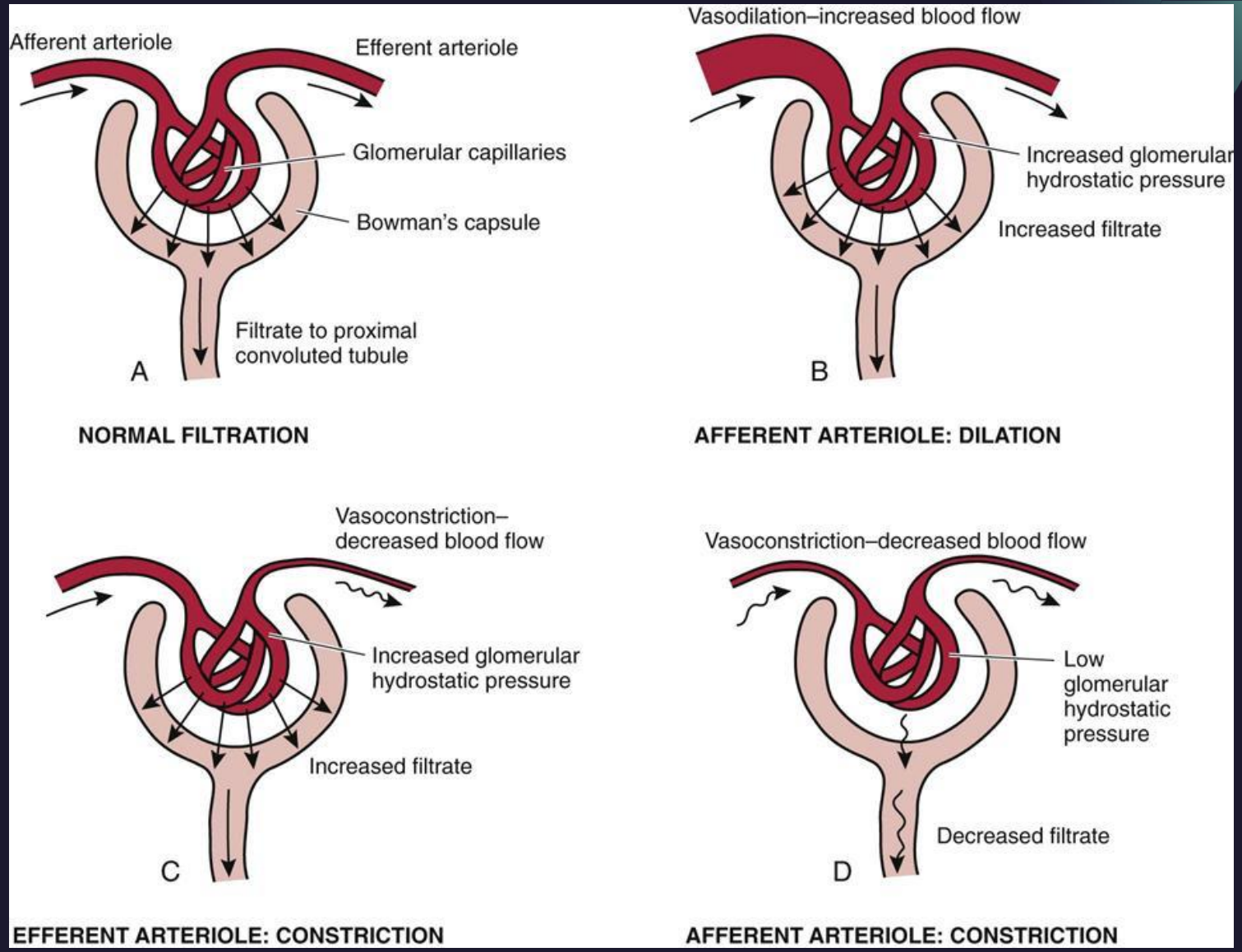
Glomerular Filtration 2

- Glomerular Hydrostatic Pressure: SBP, constriction of afferent or efferent arterioles
- Hydrostatic Pressure: Ureteric obstruction, edema/swelling of kidney in its capsule
- Blood oncotic pressure: dehydration, low plasma proteins
- Glomerular Filtration membrane: capillary permeability, effective surface area
- Hence the kidney can regulate Net Filtration Pressure by controlling the GHP
- NOTE: as fluid leaves the glomerular capillaries, the colloid pressure increases such that protein concentration is greater in the efferent arterioles than the afferent arterioles.



Renal Blood Flow Regulation

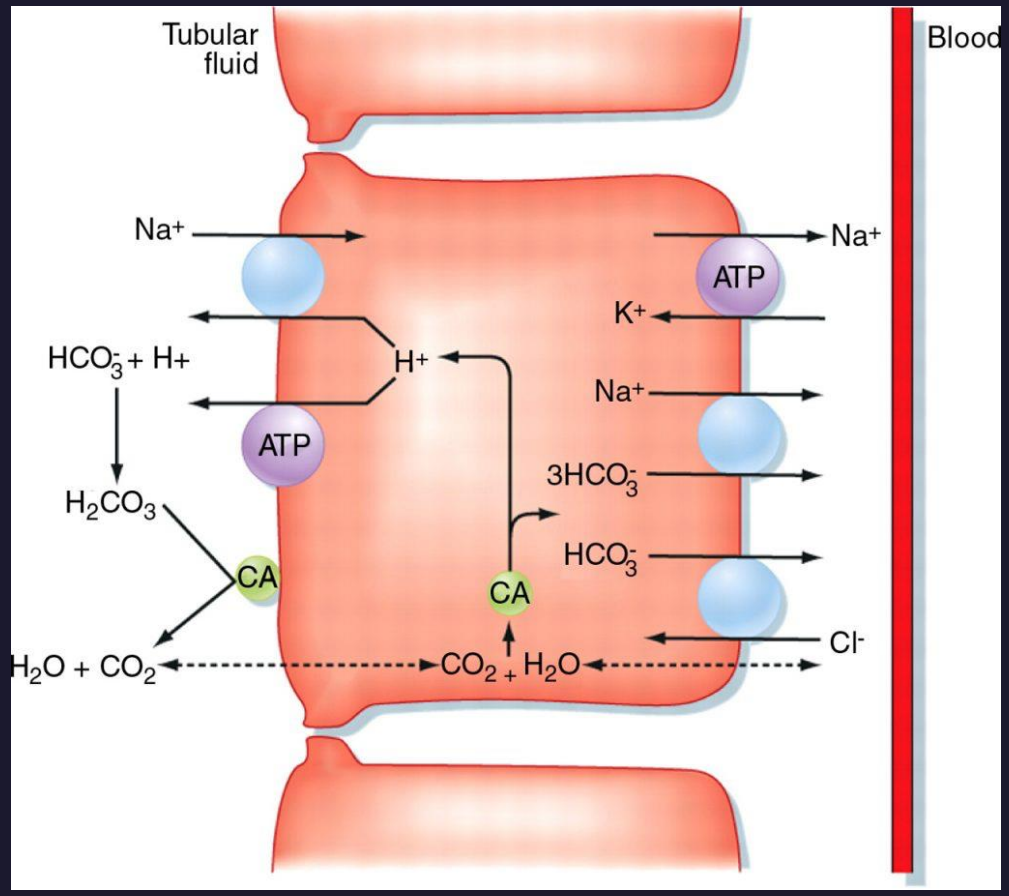
- Renal blood flow enters the glomerulus via the afferent arteriole and leaves via the efferent arteriole (whose diameter is smaller).
- Renal blood flow is regulated locally by vasoconstriction – Myogenic reflex. At normal times, this maintains a constant RBF despite variations in
- by norepinephrine (constriction, reduction of flow), dopamine (vasodilation, increases flow), angiotensin II (constricts), prostaglandins (dilation in the renal cortex and constriction in the renal medulla), and acetylcholine (vasodilation).



Tubular Reabsorption and Secretion

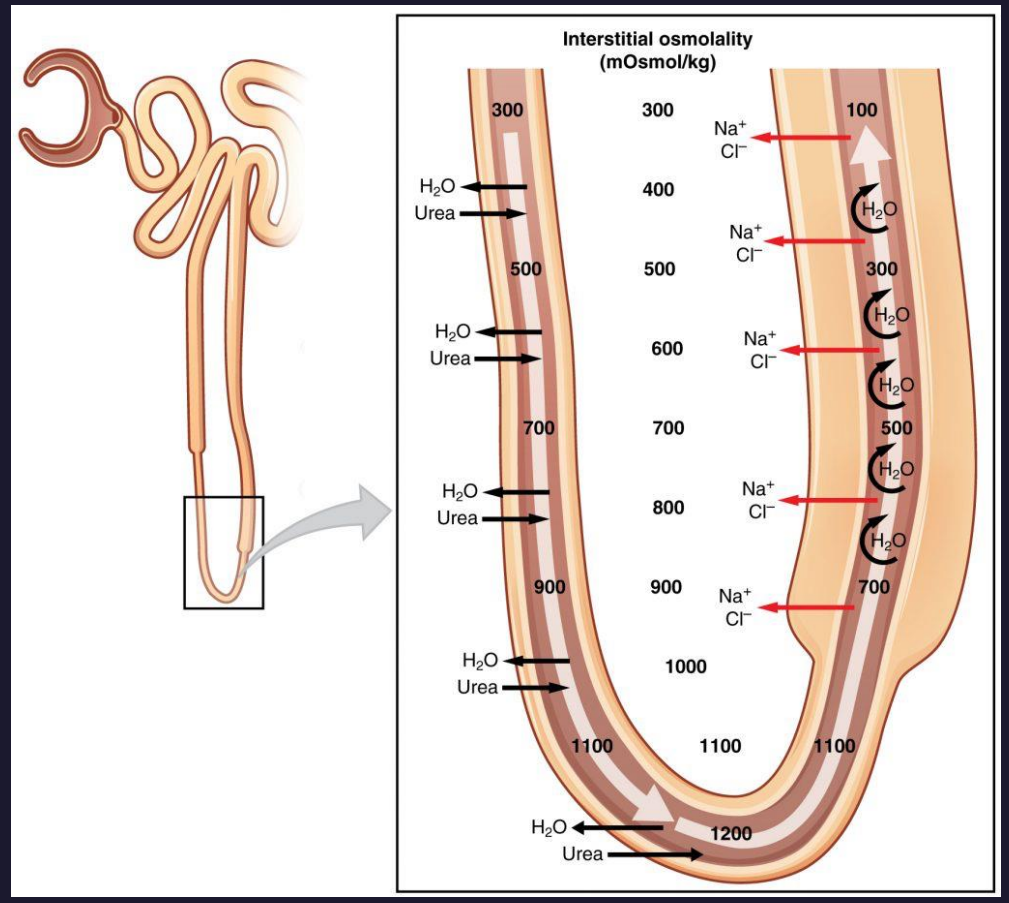
Proximal Convoluted Tubule

- Reabsorbed
  - Na – 60%. Mostly by Na/H anti-porter, Na/Glu co-transporter
  - K – 65%. Mostly active reabsorption
  - Glucose – 100%. From the tubule via Na/Glu SGLT-2 co-transporter. Into blood via GLUT-2.
  - Amino Acids – 98% reabsorbed with Na/AA co-transporter
  - Urea – 50% passively reabsorbed via simple diffusion
  - Water – 2/3 reabsorbed via aquaporin 1
  - HCO3 – 70-85% reabsorbed
  - Phosphorous reabsorbed by active transport ***PTH-dependant
- Excreted
  - H
  - Ammonium Ions



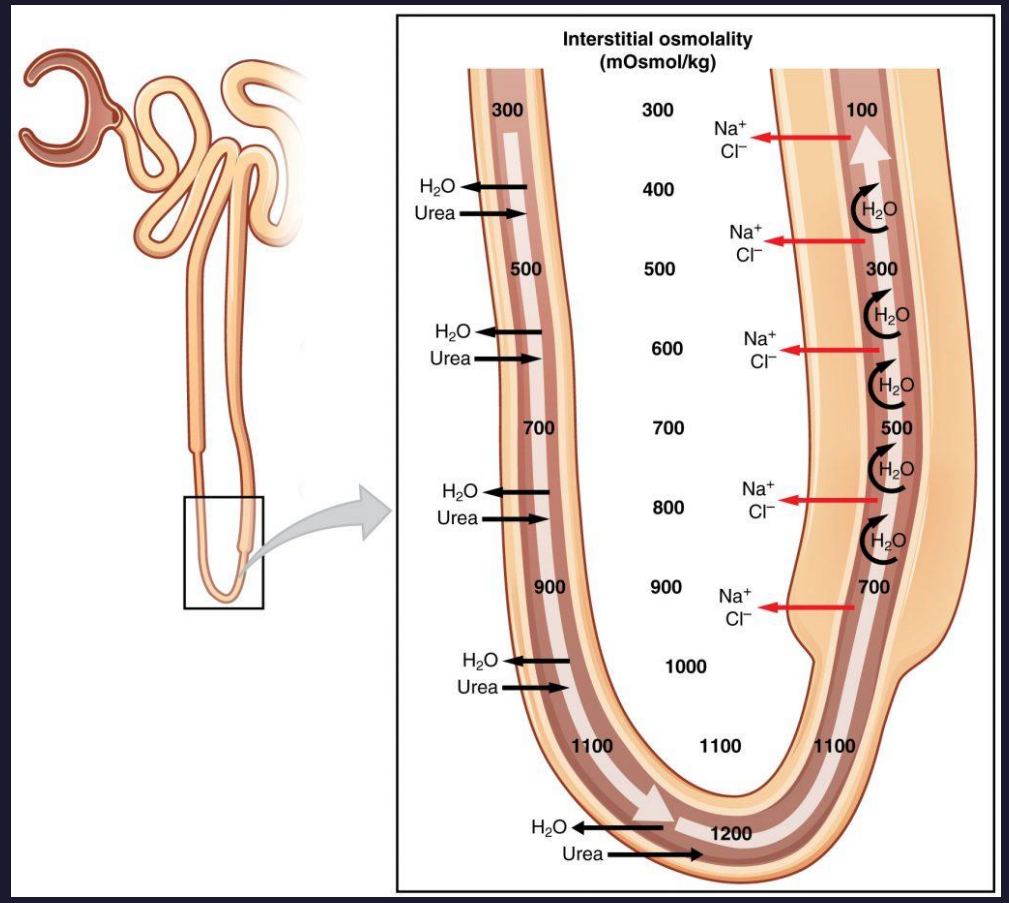
Loop of Henle

- Reabsorbed
  - Na – 30%. Mostly from lumen via N/K/Cl co-transporter. Then to interstitium via Na/K ATPase. Some transported via Na/H exchange.
  - K – 27% via the above co-transporter.
  - Cl – Via the above co-transporter.
  - Water – 10% reabsorbed in the descending limb via aquaporin 1
  - HCO3 – 10-20% reabsorbed.
- Excreted
  - H – exchanged for Na
  - Urea – 50% secreted into loop of Henle via osmotic gradient



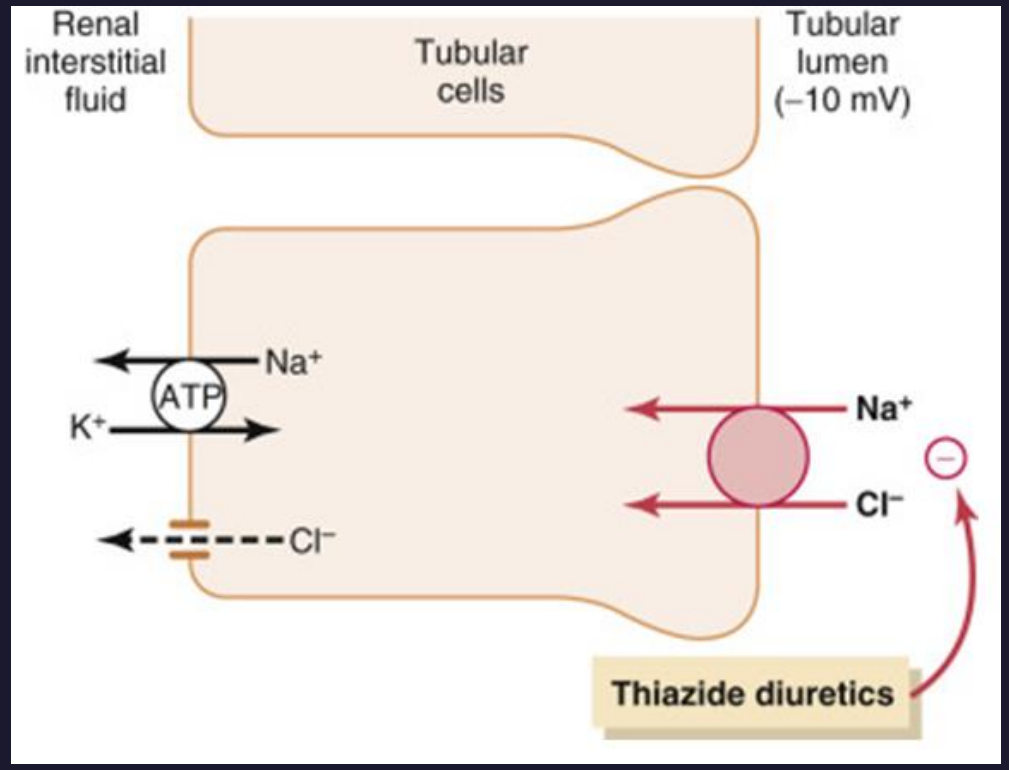
Loop of Henle – Countercurrent multiplication

- Highly water permeable **thin descending limb of the loop of Henle –** Via aquaporin 1 channels
- Water impermeable **thick ascending limb of the loop of Henle –** With active transport of Na and Cl out of the lumen
- **The thing ascending limb** allows passive reabsorption of sodium from the high molarity tubule
- As ions are actively transported into the interstitium from the THICK ASCENDING LIMB, the high ion concentration drives the water reabsorption from the THIN DESCENDING LIMB.
- This produces an increasingly high molarity tubular fluid at the lowest part of the loop (~1200mOsm/kg), further facilitating the passive reabsorption of ions.
- This mechanism maximises the osmolar concentration of the urine



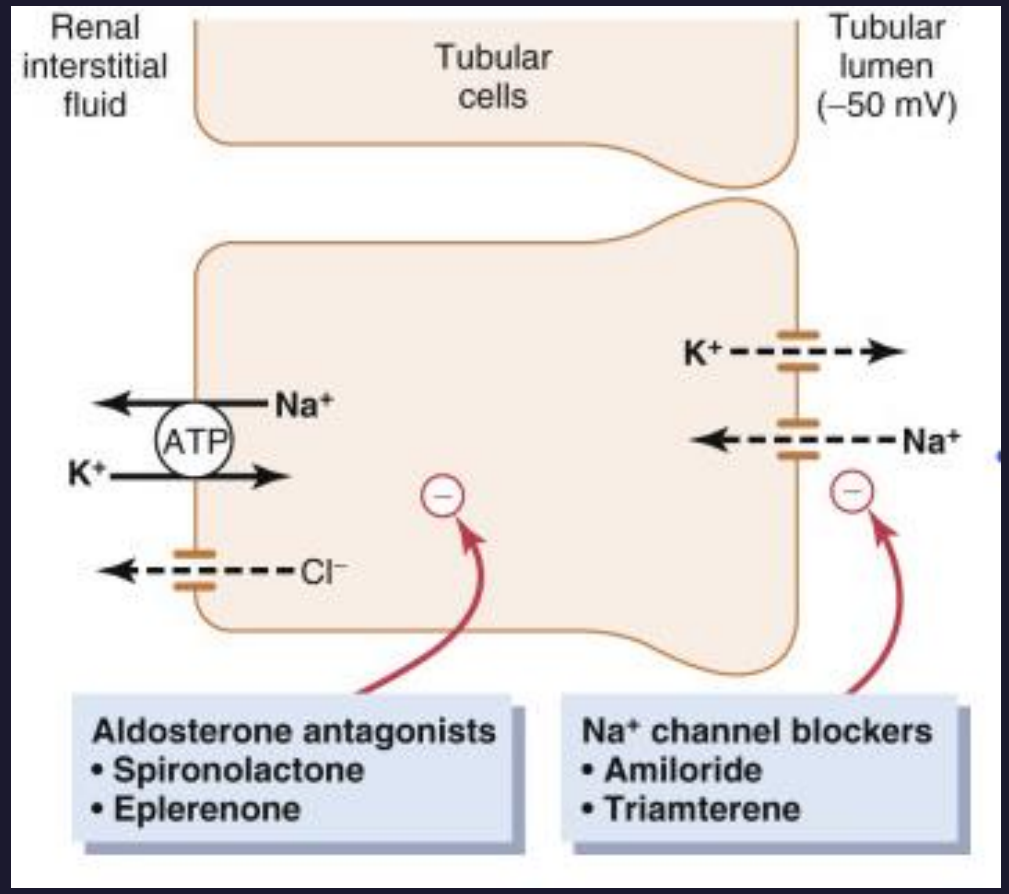
Distal Convoluted Tubule (Early)

- Reabsorption
  - Na – 7% via Na/Cl co-transporters
  - Cl – as above
  - Water – 5%
  - Ca – ***Reabsorption under direction of PTH



(Late) DCT and Collecting Duct

- Reabsorption
  - Na – In exchange for K. in PRINCIPAL CELLS. This transport is increased with Aldosterone stimulation
  - Water – resorption via Aquaporrin 2 channels: produced in response to ADH (vasopressin)
  - Ca – ***Reabsorption under direction of PTH
  - K – 15% Reabsorbed with H/K-ATPase exchangers



Fluid and Electrolyte Homeostasis

Renin, Angiotensin, Aldosterone

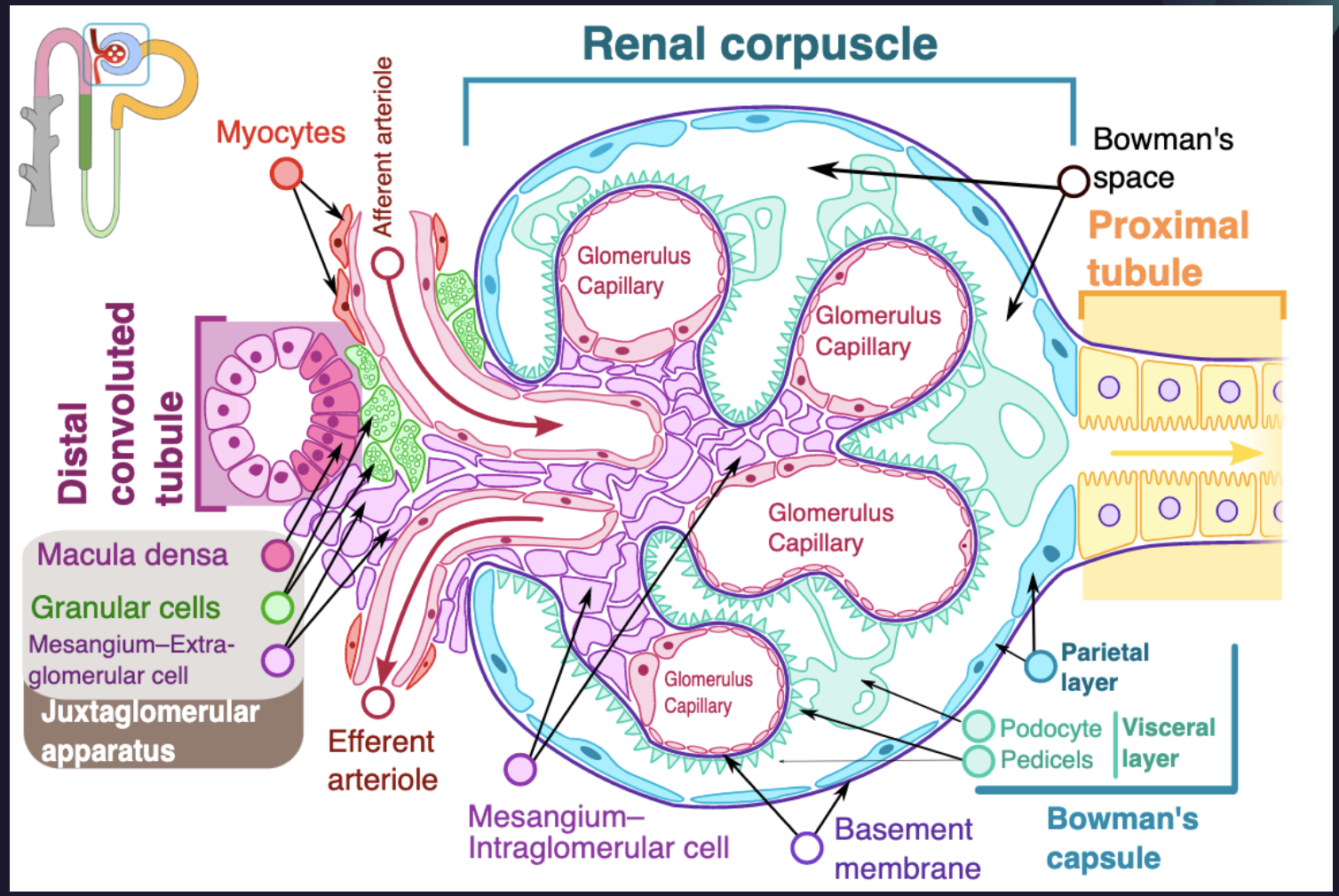
Anti-Diuretic Hormone

Potassium Homeostasis

Renin 1

- Renin is a hormone released by Juxtaglomerular Apparatus (JGA) into the blood stream
- 3 mechanisms:

1. Baroreceptor Mechanism
   - Reduced pressure in the afferent arterioles is detected by baroreceptors – Stimulate the JGA
2. Sympathetic Nerve Mechanism
   - Sympathetic stimulation of B1 adrenoreceptors in the JGA
3. Macula Densa Mechanism
   - Reduced osmolality (sodium)detected by Macula Densa cells



Renin 2

- Renin secretion is (+) by anything that:
  - Decrease ECF: dehydration, haemorrhage, diuretics, Na+ depletion
  - Decrease BP: hypotension, upright posture, cardiac failure, constriction of renal artery or aorta, cirrhosis
  - Increase sympathetic output (via renal nerves): catecholamines • prostaglandins

Angiotensin I and II

- In the Blood stream, Renin will interact with circulating Angiotensinogen (produced by theliver) – converting it into Angiotensin
- Angiotensin I is converted in the lungs by Angiotensin Converting Enzyme (ACE) into Angiotensin II in the endothelial cells of the lungs
- Angiotensin II then has multiple effects throughout the body, both renal and extrarenal.

Angiotensin II Renal Effects

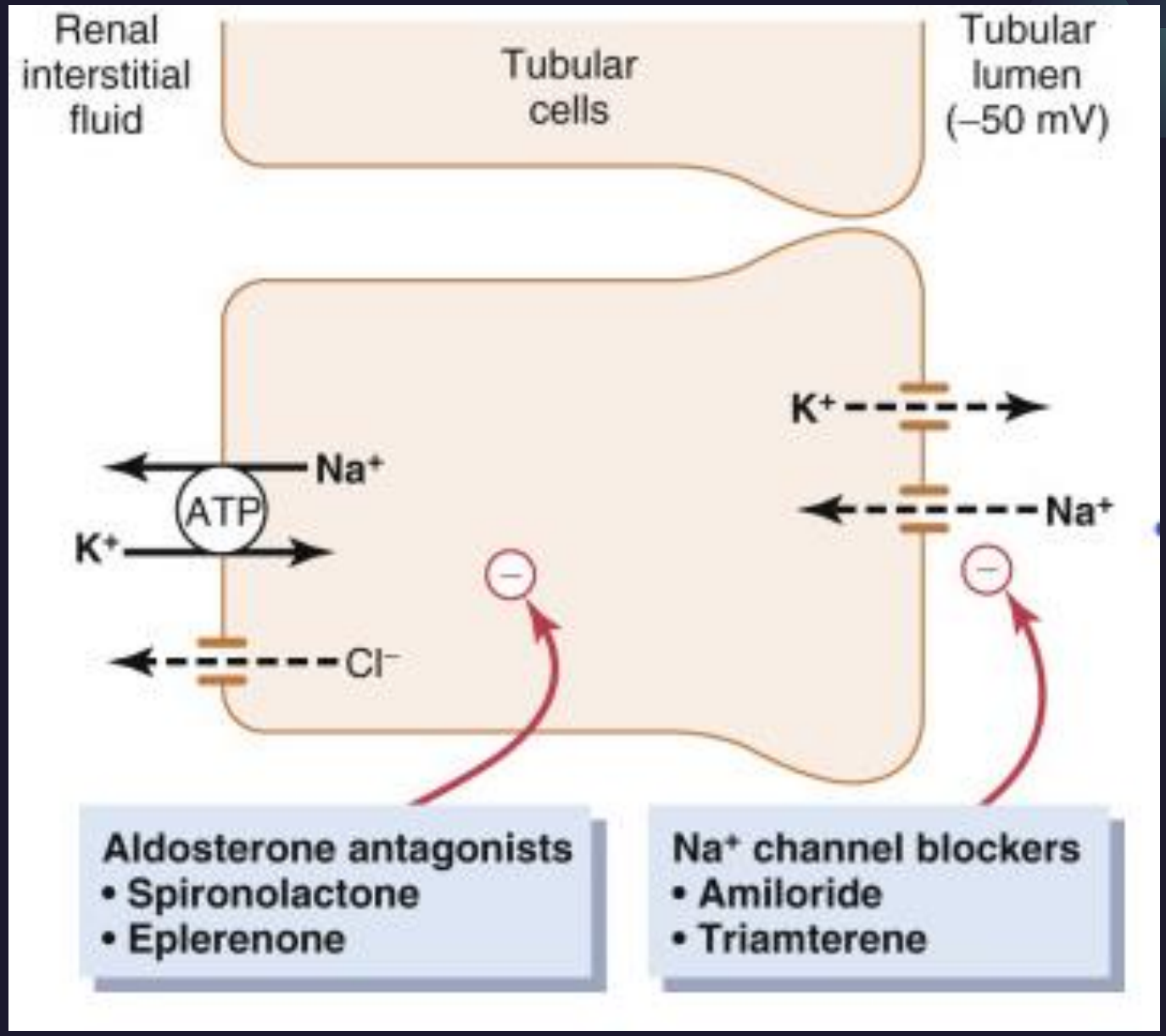
Target	Action	Mechanism
Renal artery and afferent arteriole	Vasoconstriction	Voltage-gated calcium channels open and allow an influx of calcium ions
Efferent arteriole	Vasoconstriction (greater than the afferent arteriole)	Activation of AT1 receptor
Mesangial cells	Contraction, leading to a decreased filtration area	Activation of Gq receptors and opening of voltage-gated calcium channels
Proximal convoluted tubule	Increased Na+ reabsorption	Increased Na+/H+ antiporter activity and adjustment of the Starling forces in peritubular capillaries to increase paracellular reabsorption

Angiotensin II – Extrarenal Effects

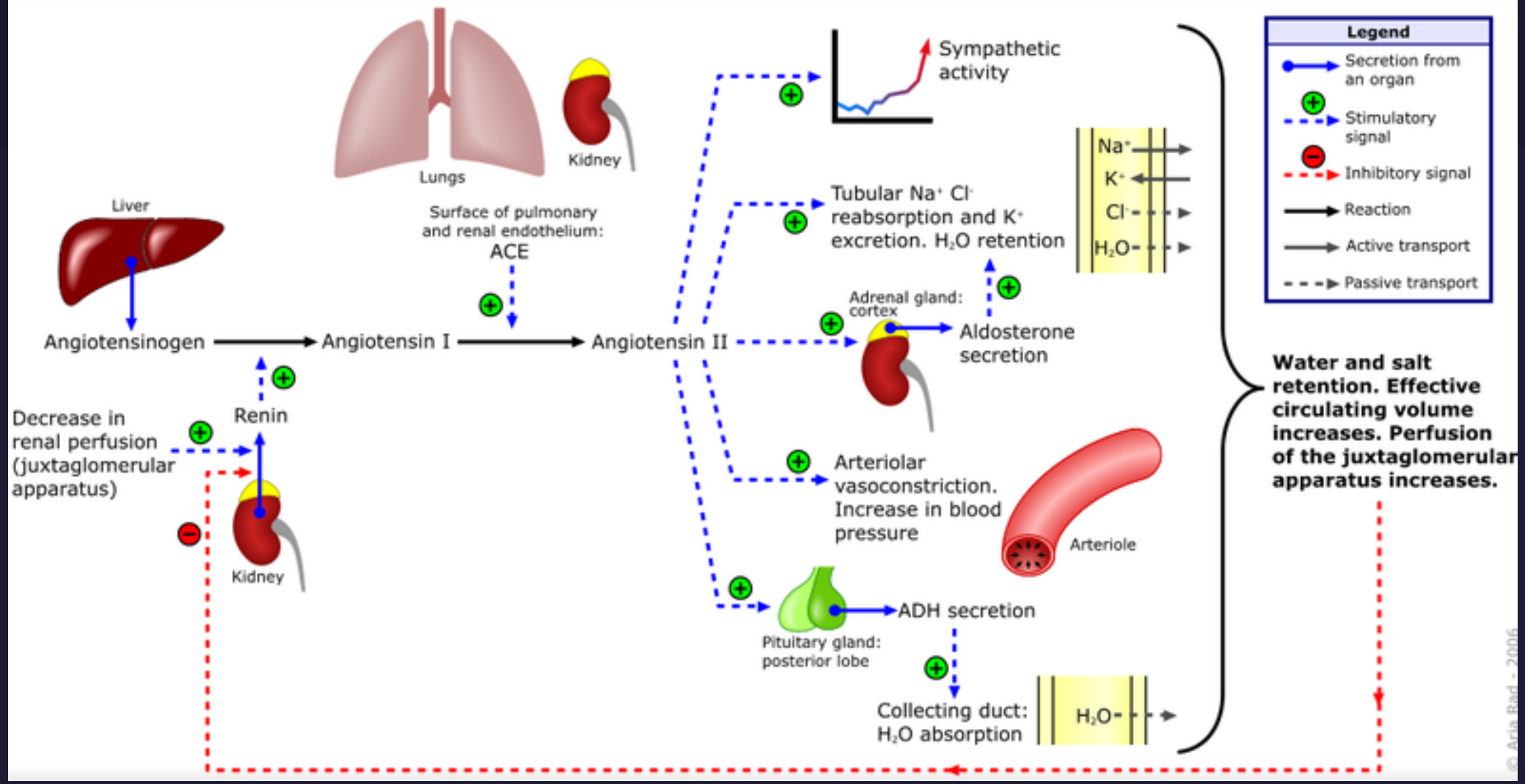
1. Vasoconstriction – Increases Systolic and Diastolic Blood Pressure. 4-8 x more effective than Noradrenaline.
2. Stimulation of the **Posterior Pituitary Gland** – Increasing the secretion of **ADH**
3. Stimulation of the **Adrenal Cortex** – Stimulates **Aldosterone** secretion
4. Stimulates the **Hypothalamus** – Produces thirst
5. Stimulates the **Sympathetic Nervous System** to release more **Noradrenaline**

Aldosterone

- Produced in the Zona Glomerulosa of the Adrenal Cortex
- Renal action: Acts on Principal Cells in the DCT and CD – exchanging Na for K and H
- Extrarenal: Stimulates reabsorption of Na by the salivary duct, sweat glands, intestines and rectum



Renin-angiotensin-aldosterone system



Antidiuretic Hormone

- ADH (AKA Vasopressin) – small peptide produced by the **Hypothalamus** and stored in the **Posterior Pituitary Gland**. From here it is secreted into systemic circulation.
- ADH is produced in response to two main stimulants

1. Increased plasma osmolality – Osmoreceptors in the **hypothalamus**
2. Reduced blood volume – Baroreceptors in the **great veins and atria**

- Effects:

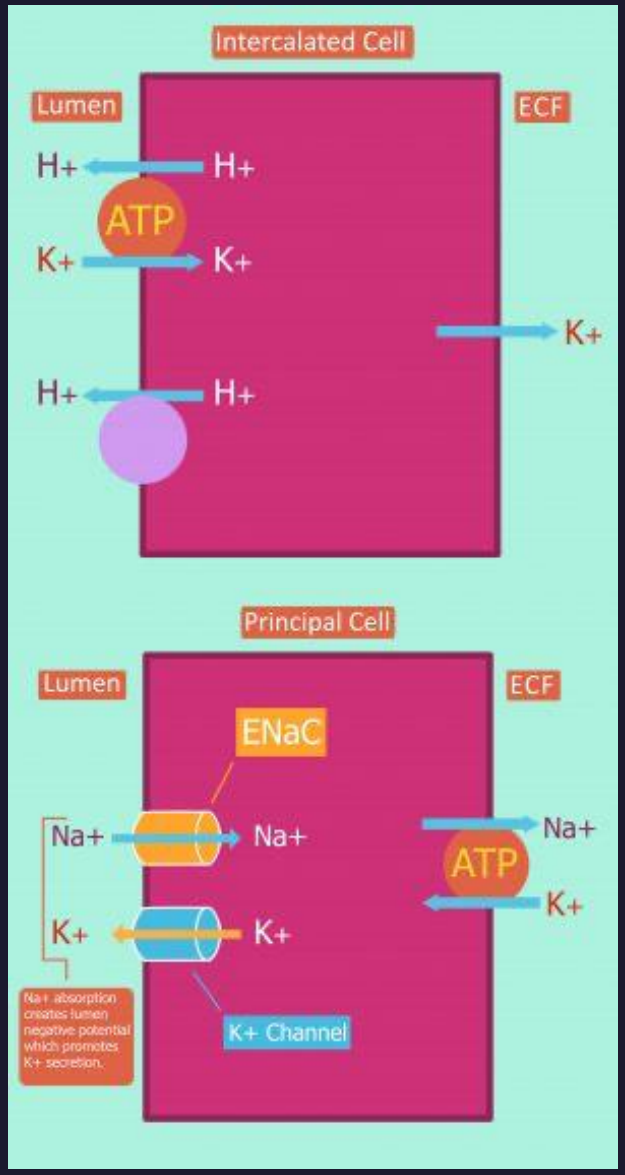
1. Stimulating the transcription and insertion of Aquaporrin-2 Channels in the **Collecting Ducts** to increase the amount of water reabsorbed – increasing total blood volume and normalising blood osmolality
2. Vasoconstriction – in high concentrations (e.g. in significant blood loss) ADH will also stimulate peripheral vasoconstriction and increase blood pressure.

Potassium Homeostasis

- An ECF potassium concentration of 3.5-5mmol/L and ICF potassium concentration of 120-150mmol/L are critical for normal cellular function.
- Muscles and Nerves: resting membrane potential
- Enzyme function, cellular growth and division
- Acid-base regulation through H/K buffer system:
  - K and H can be exchanged between cells and the ECF to maintain extracellular pH.
  - In acidosis → H enters cells in exchange for K
  - In alkalosis → K enters cells in exchange for H
  - This allows the charge between the ECF and ICF to remain stable

Potassium Homeostasis – Urinary regulation

- 90% reabsorbed in the PCT and loop of Henle as a constant. 10% variable reabsorption/secretion.
- When the body wants to preserve potassium – reabsorption occurs via the **Intercalated cells** in the DCT and CD
  - Stimulated by long-term potassium deficiency (upregulation of transporters) and acidosis
- In circumstances of high potassium - **Principal cells** will secrete potassium in exchange for sodium.
  - This occurs in high serum potassium , high aldosterone secretion and changes in pH
- metabolic acidosis. H+ move into cell, K+ move out of cell plasma K+ rises. increase K+ secretion in distal tubule. Total body K depleted, despite high plasma K+.
- metabolic alkalosis. H+ move out of cell, K+ move in. Low plasma K+ (initially). However, chronic alkalosis may lead to loss of body K because of increased K secretion by renal Principal cells.

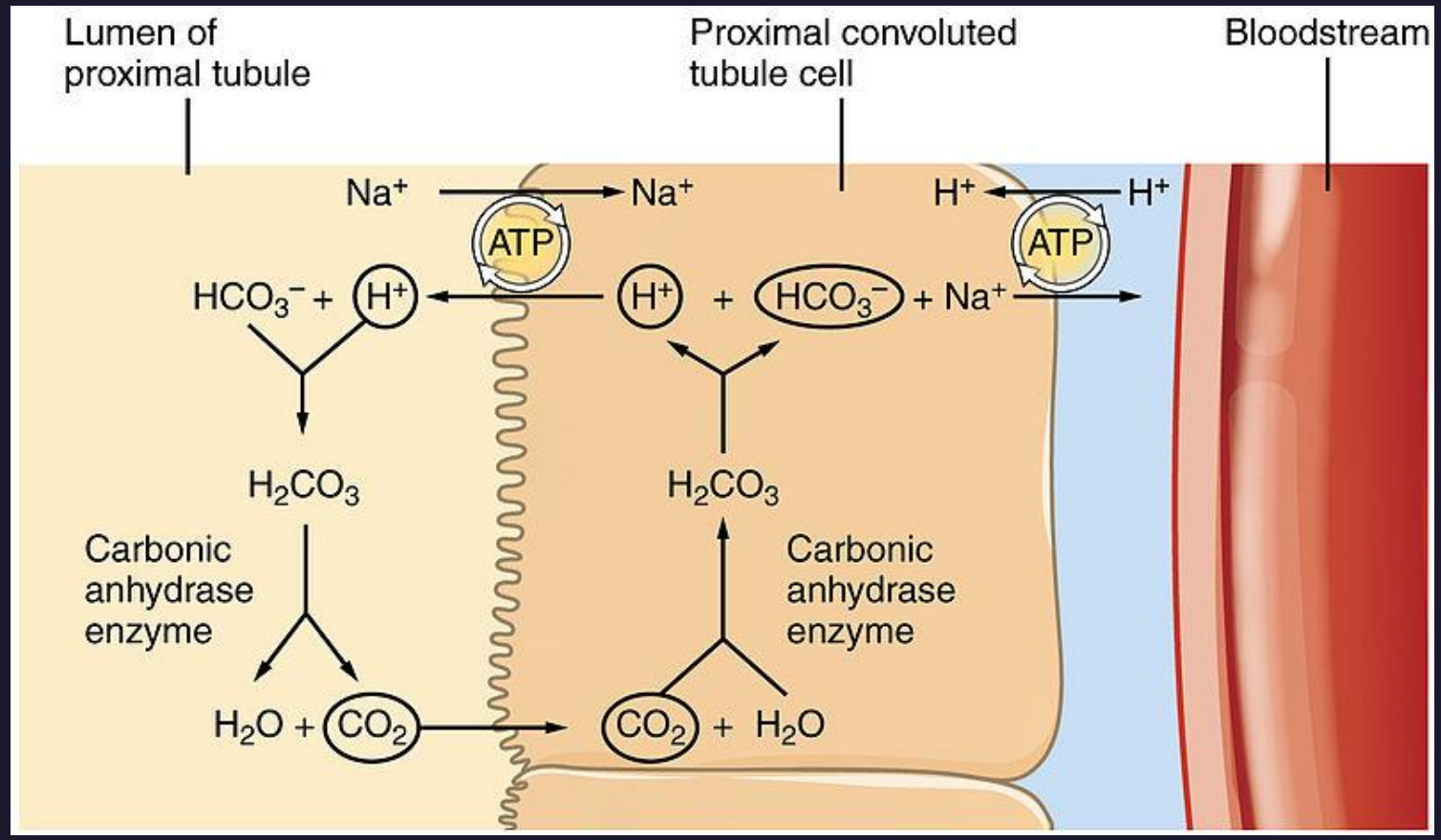


Urinary regulation of the Acid-Base Balance

- Blood pH can be regulated in the nephron through 2 mechanisms:

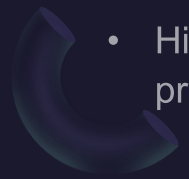
1. Active excretion of Hydrogen ions: transported into the lumen where they can be bound with HPO4 to make H2PO4 (dihydrogen phosphate) or with NH3 (ammonia) to make NH4 (ammonium)

2. **Bicarbonate Reabsorption**



Diuresis

- Water Diuresis
  - High water intake → lower plasma osmolality → low/suppressed ADH secretion (Baroreceptors, osmoreceptors)
  - CD becomes impermeable to water → excess water is lost in urine
  - Normal GFR is preserve and the constant water reabsorption rate of the PCT, Loop of Henle is preserved → maximal urine flow is approx. 16ml/min
- Osmotic Diuresis
  - Occurs when a solute exists in the tubules which cannot be reabsorbed.
  - E.g. Mannitol, Glucose in T1DM, ions (Na, Cl) with traditional diuretics (e.g. thiazides, loop diuretics)
  - High osmolality of tubular fluid prevents the normal reabsorption of water in the PCT/LOH meaning very high urine flows can be produced.



Practice Question

13569 – Aldosterone increases the reabsorption of sodium from the
1: collecting duct
2: saliva
3: sweat
4: small intestine

TTTT

Practice Question

22374 – Angiotensin II produces
1: arteriolar constriction
2: a rise in diastolic blood pressure
3: increased water intake
4: inhibition of adrenocorticotrophin hormone (ACTH) secretion

TTTT

Practice Question

10144 – In the kidney
1: potassium is largely reabsorbed in the proximal tubules
2: urea is actively reabsorbed from the tubules
3: glucose is removed from the glomerular filtrate by active transport
4: protein concentration of blood in efferent arterioles is the same as that in afferent arterioles

TFTF

Practice Question

14631 – Renal blood flow falls in
1: hypovolaemia
2: stimulation of A1 adrenergic receptors
3: stimulation of the vasomotor area in the medulla oblongata
4: exercise

TTTT