RENAL PHYSIOLOGY

FUNCTIONS OF THE KIDNEYS

- **Regulation of extracellular fluid volume and blood pressure** - *works with CV system to ensure tissues get enough oxygen and BP is within normal values*
  ECF fluid ↓ ⟶ *BP* ↓ ⟶ If they fall too low ⟶ blood flow ↓

- **Regulation of osmolarity** – *blood osmolarity needs to be maintained around 290mOsM (with behavioral drives, such as thirst)*

- **Maintenance of ion balance** - balancing dietary intake with urinary loss to maintain proper levels of Na^+, K^+ , Ca^{2+} .

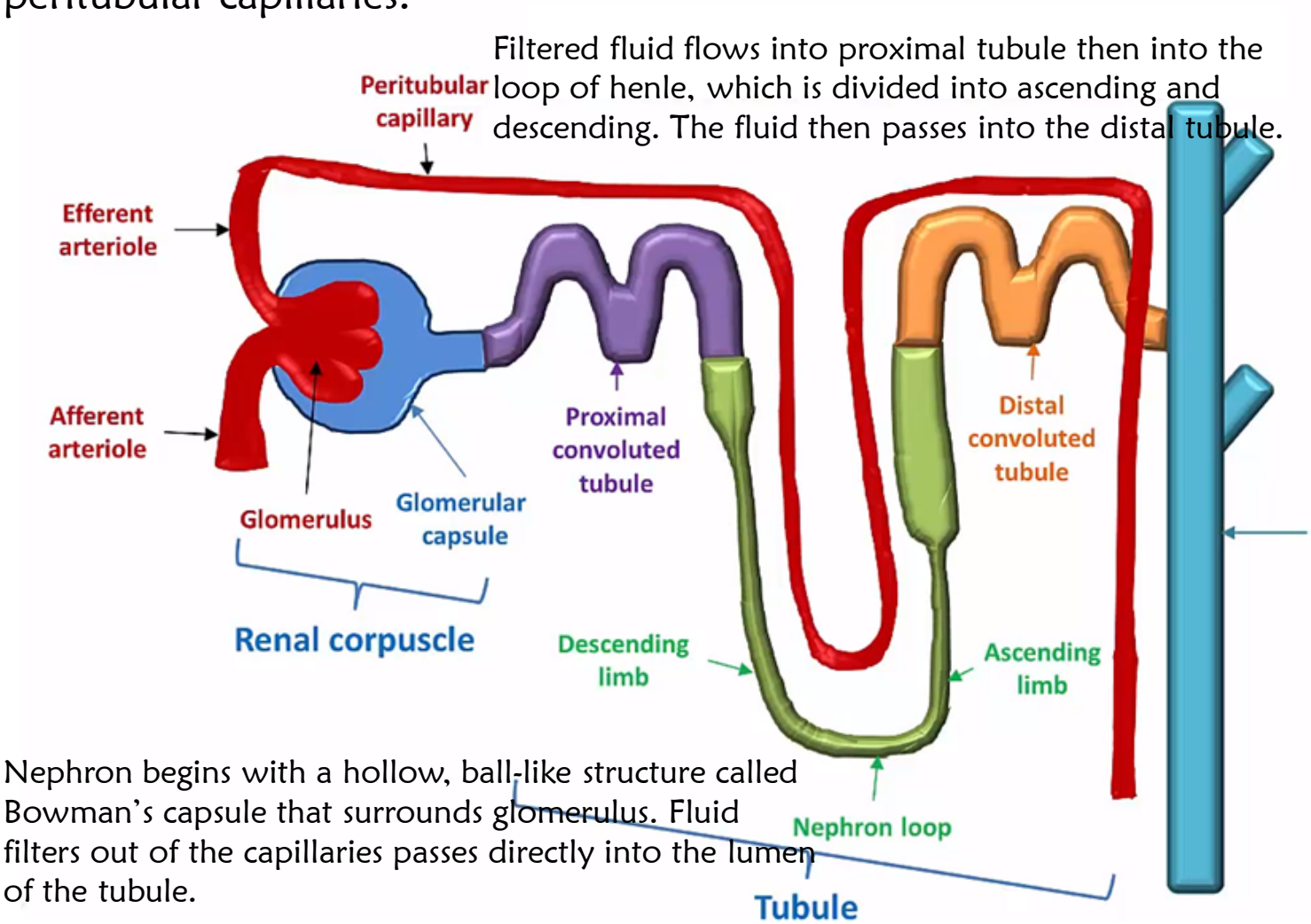
- **Homeostatic regulation of pH** – *they remove either H^+ or HCO_3^- as needed*
  ECF becomes acidic ⟶ *H^+* removal, *HCO_3^- conservation*
  ECF becomes alkaline ⟶ *HCO_3^-* removal, *H^+ conservation*

- **Excretion of wastes** – *removes waste molecules dissolved in the plasma like urea and uric acid (nitrogenous wastes), urobilinogen (Hb metabolite, yellow color), creatine (from muscle metabolism), xenobiotics (foreign substance)*

- **Production of hormones** – *erythropoietin (regulates RBC production), renin (influence* Na^+balance and *BP) and calcitriol (regulates Ca^{2+} balance)*

•Kidneys modify the composition of the fluid.
•Modified fluid is called urine, leaves the kidney
•And passes into a hollow tube called ureter. There are two ureters, one leading from each kidney to the urinary bladder.
•The bladder expands and fills with urine until a reflex called micturition or urination, the bladder contracts
•and expels urine through a single tube, urethra.

To filter the blood out of the blood and into the lumen of the nephron at the glomerular capillaries, then to reabsorb fluid from tubule lumen back into the blood at the peritubular capillaries.



Filtered fluid flows into proximal tubule then into the loop of henle, which is divided into ascending and descending. The fluid then passes into the distal tubule.

Nephron begins with a hollow, ball-like structure called Bowman's capsule that surrounds glomerulus. Fluid filters out of the capillaries passes directly into the lumen of the tubule.

The fluid then passes into the distal tubule. Distal tubules up to 8 nephrons drain into a larger tube called collecting duct. They pass from cortex through medulla and drain into renal pelvis. It is now called urine and flows the ureter to excretion.

Twisted configuration of nephron causes the ascending limb of loop of Henle to pass between afferent and efferent arterioles.

The macula densa is a collection of specialized epithelial cells in the distal convoluted tubule that detect sodium concentration of the fluid in the tubule.

This region is known as juxtaglomerular apparatus.
Its main function is to regulate blood pressure and the filtration rate of the glomerulus.

Tubuloglomerular Feedback

Juxtaglomerular cells and Macula densa monitor blood flow and blood pressure along the arterioles. They send chemical signals needed to restore the proper filtration rate

Twisted configuration of nephron causes the ascending limb of loop of Henle to pass between afferent and efferent arterioles.
Tubule and arteriolar walls are modified in the regions where they contact each other and together form **juxtaglomerular apparatus.**
The modified portion of the tubule epithelium is a plaque of cells called **macula densa.**
The adjacent wall of the afferent arteriole has specialized SMC called **granular cells.** They secrete renin, an enzyme involved in salt and water balance.

Reabsorption

Principles governing the tubular reabsorption of solutes and water. Sodium and water always follow each other.

Transepithelial (transcellular**) transport-** *(passing through cells)*-Substances cross both apical and basolateral membrane

Paracellular pathway *(passing around cells)*-Substances pass through the junction between two adjacent cells

Renal Transport can reach **saturation**

Maximum rate of transport occurs when all available carriers are occupied by substrate.

Transport rate is proportional to plasma concentration until transport saturation=renal threshold

SECRETION

The transfer from ECF to the lumen of the nephron.
Secretion of H^+ and K^+ in distal nephron is important.
Secretion enhances excretion of a substance (*adds to the substances collected during filtration, making excretion more effective)*
It is an active process.

EXCRETION

The result of all processes.
By the time, the fluid reaches the end of the nephron, it has little resemblance to the filtrate that started in Bowman's capsule.
Glucose, aminoacids and useful metabolites are gone (reabsorbed), organic wastes are more concentrated.
The concentration of ions and water are variable, depending on the state of the body.
Excretion = filtration – reabsorption + secretion

CLEARANCE

Clearance of a solute is the rate at which that solute disappears from the body by excretion or by metabolism.
Non-invasive way to measure GFR
Inulin and creatinine are used to measure GFR

$$Cl_R = \frac{\text{Rate of urinary excretion}}{\text{Plasma drug concentration}}$$

$$Cl_R = \frac{\text{Rate of (filtration + secretion – reabsorption)}}{\text{Plasma drug concentration}}$$

By comparing the creatinine level in urine with the creatinine level in blood, this test estimates the glomerular filtration rate (GFR). GFR is a measure of how well the kidneys are working, especially the kidneys' filtering units.

All solutes have same concentration in the blood 4 molecules/100 ml. GFR is 100 ml/min.

100% glucose is reabsorbed so glucose clearance is zero.

Urea is partially reabsorbed. 2 molecules are excreted, so urea clearance is 50 mL plasma.

Penicillin is filtered and not reabsorbed. Additional penicillin molecules are secreted. + are filtered but 6 are excreted so its clearance is 150 ml plasma.

Micturition

The storage of urine and the micturition reflex

Once filtrate leaves collecting ducts, is called **urine** flows into renal pelvis and down to ureter to the bladder with smooth muscle contractions.

In bladder, urine is stored until relased in the process known as **urination**, **voiding** or **micturition**.

Internal is a continuation of bladder wall and normal tone keeps its contracted.
External is a ring of skeletal muscle and controlled by somatic neurons. Tonic stimulation maintains contraction except during urination.

Mass Balance in the Body

- Homeostasis requires that amounts gained must be equal to that lost.
- **Ion concentration-** need proper amounts of Na+, Cl-, K+, and Ca2+:
  - **nervous, cardiac& muscle function-** *imbalances cause problems with membranes of cells that are excitable.*
  - **Primarily replaced with thirst & appetite and excreted in urine, sweat, & feces**
- **pH balance-** cells functions within a pH range that is maintained by H+, CO2, & HCO3–
- **Fluid**- water levels need to be maintained, ingestion and urine formation have largest impact.

Key factors for Homeostasis

- **Na+ & H_2O= affect ECF**
  - **Osmolarity:** amounts of solutes dissolved in solution, concentration and permeability influence direction of osmosis which changes the size of cells

Balance process is integrative

The body's integrated response to changes in blood volume and blood pressure incorporate many systems

Decreased blood volume will result in mechanisms that increase blood pressure and volume, and reduce water loss

Fluid and Electrolyte Homeostasis

Increased blood volume results in the excretion of salt and water which eventually reduces blood pressure and ECF/ICF volumes.

Water Balance

A model of the role of the kidneys in water balance

Kidneys cannot add water, only preserve it or get rid of excess amounts. Renal filtration will stop if there is a major loss causing extremely low blood pressure and blood volume

When homeostasis needs eliminating excess water, urine gets diluted.
Removal of excess water is called **diuresis**. Diuretics promote excretion of water.
When kidneys need to conserve water, urine gets concentrated.

Water Reabsorption

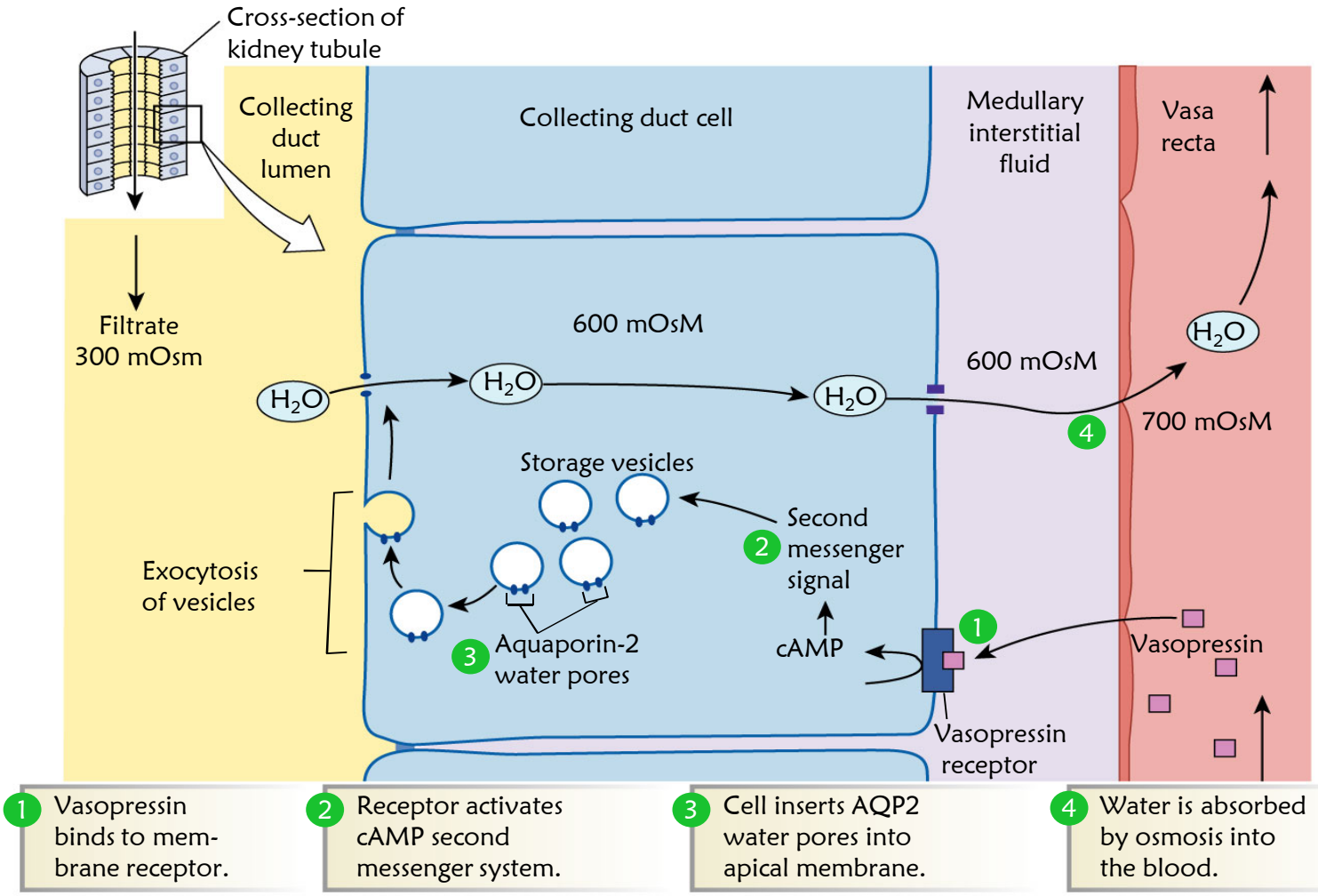
Vasopression or antidiuretic hormone causes a graded effect of forming water pores on collecting duct cells. Thus permeability is increased and more water is retained making urine more concentrated.

Water Reabsorption

If vasopressin is absent water will not move out through water pores (aquaporins) and the urine will be dilute.

Vasopressin is also called antidiuretic hormone- it causes reabsorption of water (in turn increasing urine concentration and decreasing volume).

Water Reabsorption



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Factors Affecting Vasopressin Release

Three stimuli control vasopressin but the most potent is blood osmolarity above 280mOsM. The higher the osmolarity, the more vasopressin released by posterior pituitary.
Osmoreceptors also trigger thrist centers in hypothalamus

Countercurrent exchange

Blood flow moves in the **opposite direction** from filtrate flow in the loops of Henle.
Descending limb is **permeable to water** does not transport ions.
Filtrate becomes more concentrated.
Ascending limb is **impermeable to water** while actively transporting Na^+, K^+, Cl^- (NKCC symporter)

Sodium Balance

We ingest a lot, 9 g NaCl per day. Our normal NA is 135-145 miliosmoles Na per liter.
Addition of NaCl raises osmolarity. This trigger 2 responses.
Concentrated urine.

Homeostatic responses to salt ingestion show the integrated effects on sodium, water, and blood pressure. Without salt appetite [salt] would increase and tissue cells would shrink. Thus vasopressin and thirst is activated.

ALDOSTERONE

Reabsorption of Na^+ in distal tubules and collecting ducts is regulated by aldosterone. More aldosterone means more Na^+ reabsorption. Aldosterone also affects NKA activity and causes K^+ secretion.

Decreased blood pressure stimulates renin secretion.

Granular cells can be activated to release renin by three factors:
drop in blood pressure,
a signal from the kidneys,
increased sympathetic activity.

The renin-angiotensin-aldosterone pathway-(RAAS).

Renin is an enzyme that assist in ANG II formation. ANGII activates several mechanisms that ultimately increase blood pressure and volume

Action of natriuretic peptides- *cause sodium loss through urine (natriuresis) and act as RAAS antagonist. They are released when myocardial cells stretch too much or during heart failure*

Potassium Balance

- Regulatory mechanisms keep plasma potassium in narrow range (3.5-5meq/L)
  - Aldosterone is released in response to excess levels, it increases permeability at distal nephron so K^+ is moved into the urine while sodium is reabsorbed