Distal tubule

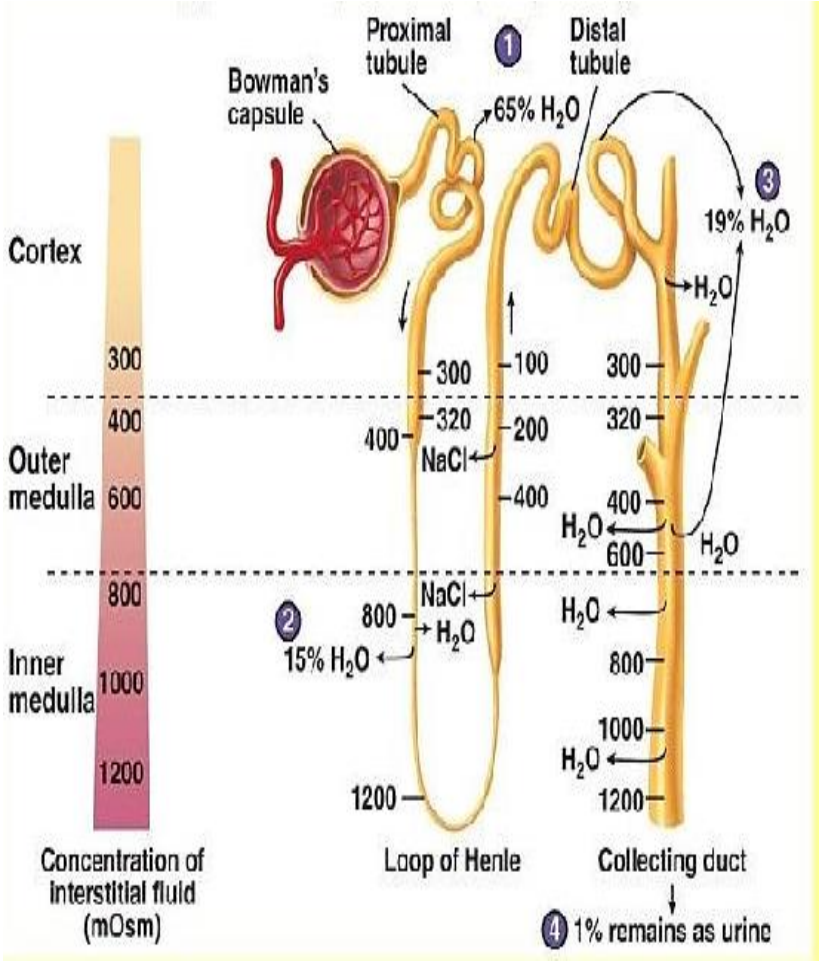
- Osmotic pressure of the filtrate is less than the surrounding plasma. Some water diffuse out and some salt diffuse in to return osmotic pressure to **300 mOsm**.
- **Aldosteron**e acts in this section by activating Na^+/K^+ pump .

Collecting duct

- There are two types of cells:

1. **The principle cells** reabsorb Na^+ and secret K^+ in the presence of ADH, also reabsorb water.
2. **The intercalated cells** secret H^+ and reabsorb HCO_3^- .

- As the collecting duct passes through the deepest layer of the medulla (which have very high concentration of NaCl) the maximum reabsorption of water occurs (by osmotic), raising the osmotic pressure of the filtrate to over 1200 mOsm.
- In the presence of ADH , water passes through the cells from the lumen to the interstitial fluid down the osmotic gradient.



The countercurrent mechanism

- The kidney's ability to establish an osmotic gradient rest primarily in the loop of Henle , and vasa recta through the **countercurrent system**.
- **Active transport of NaCl** from the ascending limb of Henle and **urea trapping** within medullary interstitium are factors that countercurrent system depend on .

Urea trapping

- Urea contributes to the medullary concentrating gradients. It is freely filtrated in the glomerulus and partially reabsorbed in the proximal tubule .
- The cortical and medullary portions of the collecting tubule are **impermeable** to urea, whereas the inner medullary collecting tubules are **permeable** to urea.
- In the presence of **ADH** , urea concentration in the collecting tubules becomes high due to removing of water through open channels. ADH increases the permeability of inner medullary collecting tubule to urea allowing more urea to diffuse into the medullary interstitial causing more hypertonic medulla .

Potassium excretion

- Most potassium is intercellular (**140mmol/L**), while extracellular plasma concentration is kept low (**4mmol/L**) to maintain the resting potential of the body cells.
- The distribution of Na^+ and K^+ between the intercellular and extracellular compartments is maintained by Na^+/K^+ ATPase pump which moves Na^+ out and K^+ into the cells.
- The kidney plays a major role in the regulating K^+ excretion .
- Acute renal failure results in hyper kalmia due to decrease ability of the kidney to excrete K^+ .
- Distal tubule and collecting tubule secret K^+, and aldosterone increase the activity of Na^+/K^+ pump.

Renal regulation

1. The sympathetic noradrenergic fiber supply the afferent, efferent arterioles and tubules.

- A strong increase in the renal sympathetic cause vasoconcentraction to the afferent arterioles by the baroreceptors reflex and renal blood flow decreases. Although the GFR .
- An increase in the renal sympathetic activity results in direct increase reabsorption of Na^+ by the proximal tubule.
- An increase in sympathetic activity stimulates rennin secretion and angiotensin II production.

2. Rennin- angiotensin system

- Rennin is an enzyme that is synthesized, stored and secreted in a specialized region (the juxtaglomerular apparatus).
- Rennin is stimulated by factors:

1. Increased renal sympathetic activity.
2. Reduced renal perfusion pressure.

3. Decreased NaCl delivery to the **macula densa**, these cells respond to change in the composition of the tubular fluid.

- Renin splits the **angiotensin I** from **angiotensinogen**. Angiotensin I is then converted to **angiotensin II** by **angiotensin converting enzyme** (**ACE**) in the vascular endothelium.
- Angiotensin II has the following effects:

1. It causes vasoconcentraction

- **In the systemic circulation**, it increases arterial blood pressure.
- **In the kidneys,** it constricts the efferent arterioles raising the pressure in glomerular capillaries and help in GFR.

2. It stimulates Na^+ reabsorption by the proximal tubule the Cl^- and water.
3. It stimulates the **aldosterone** secretion by the **adrenal cortex**.
4. It stimulates **ADH** secretion from the posterior **pituitary gland** .
5. It stimulates thirst by an action on the brain.

3. Prostaglandins

- Prostaglandins are **localized hormone** . Their synthesis is increased by renal sympathetic activity, when angiotensin II levels are high and when rennin release is stimulated.
- Renal prostaglandins are vasodilator help to prevent excessive reduction in renal blood flow.

4. Aldosterone

- Aldosterone is a hormone synthesized and secreted by the **adrenal cortex** .
- It is stimulated to release when the concentration of angiotensin II and plasma K^+ increase.
- It acts within the kidney to stimulate Na^+ absorption and K^+ secretion by the distal tubule and collecting duct.

5. Atrial natriuretic peptide

- **Atrial natriuretic peptide (ANP)** is a polypeptide hormone synthesized and released by the **myocardial cells** of the atrium.
- **ANP** tends to oppose the rennin-angiotensin system action:

1. Vasodilatation within the kidney.
2. Inhibition of aldosterone secretion.
3. Inhibition of ADH.

6. Antidiuretic hormone (ADH)

- ADH is released from the **posterior pituitary** gland .
- Its secretion is stimulated by an increase in plasma osmolality and decrease in the arterial blood pressure.
- ADH has the following effects:

1. Vasoconstriction of arterioles of the systemic circulation (including the kidney) .
2. It increases water reabsorption by the kidney (↑ water permeability of the collecting duct).
3. It increases the urea permeability of the medullary portion of the collecting duct.

7. Parathyroid hormone (PTH)

- **Parathyroid hormone (PTH)** is secreted by the **parathyroid gland**.
- It secretion is stimulated by decrease in the concentration of plasma Ca^{+2} .
- PTH stimulates the production of **calcitriol** which increases Ca^{+2} phosphate absorption from the gastrointestinal tract and stimulates bone reabsorption.
- In the kidney, PTH stimulates Ca^{+2} reabsorption by the thick ascending limb of loop of Henle and distal tubule, raising the Ca^{+2} plasma level.

Renal clearance

- Renal clearance refers to the volume of plasma that is cleared of substance in minute. Renal clearance tests are done to determine the GFR which detect glomerular damage and follow the progress of renal disease.
- The renal clearance rate (RC) of any substance, in ml\min, is calculated from the equation:

RC=UV/P where U=concentration of the substance in urine (mg/ml) , V=flow rate of urine formation (ml/min) , P= concentration of the substance in plasma (mg/ml).

- Because it is freely filtrated and neither reabsorbed nor secretion by the kidney , insulin is the standard used to determine the GFR, insulin has a renal clearance value equal to the GFR.
- When insulin is infused such that it's plasma concentration is 1 mg/ml (P=1mg/ml), U=125mg/ml, and V=1ml/min, therefore it's renal clearance is CR=(125*1)/1 =125 ml/min, meaning that in 1 minute the kidneys have removed(cleared) all the insulin present in 125 ml of plasma.
- A clearance value less than that of insulin means that a substance is reabsorbed . An example is urea with an RC of 70 ml/min, meaning that the 125ml of glomerular filtrate formed each minute, 70 ml is completely cleared of urea, while the urea in the remaining 55ml is recovered and returned to the plasma .
- If the RC is zero (such as for glucose in healthy person), reabsorption is complete or substance is not filtrate.
- If the RC is equal to that of insulin, there is no net reabsorption or secretion.
- If the RC is greater than that of insulin, the tubule cells are secreting the substance into the filtrate. This is the case with most drug metabolites.