<u>Process of urine Formation</u>

• About **1200 ml** of blood reach kidney/ minute i.e., containing about **700 ml** plasma and these are called "renal plasma flow" .

• Of these 700 ml plasma about **125 ml** of protein free plasma are filtered from the glomerular membrane and reach renal tubules and they are called the glomerular filtration rate" (GFR).

• The rest of the plasma (700-125= 575 ml) return back to the efferent arterioles and runs, through the Peri-tubular capillaries, side by side with the glomerular filtrate in the kidney tubules.

• After filtration in glomeruli, renal tubules do the following processes:

a) **<u>Reabsorption:</u>** Definition: reabsorption is the movements of substances from lumen of renal tubules crossing tubular cells back to the blood.

• Certain substances undergo complete reabsorption as amino acids & glucose, while other undergoes partial reabsorption as Na^+ , K^+ , HCO_3^- .

• 99% of the Glomerular filtrate is reabsorbed.

• Solute reabsorption occurs by: * Active mechanism: against electrochemical gradient as glucose & amino acids. * Passive mechanisms: under electrochemical gradient.

<u>b) Secretion</u>: Definition: Secretion is the movement of substances from blood surrounding the tubules to the tubular lumen to be excreted with urine.

•Secretion may be complete (all substance that enter kidney is excreted in urine (e.g., injected PAHA) or may be partial secretion (e.g., H^+ ion or K^+).

•Secretion may also be active or passive & has a transport maximum.

<u>c) Synthesis</u>: Definition: Synthesis is the formation of new substances as ammonia (for H^+ regulation).

<u>d) Excretion</u>: Definition: Excretion is the final substances that are found in urine.

• Only 1 ml/minute of 125 ml filtered fluid is excreted as urine (in normal adult = 1500 ml/day in normal adult).

• Urine contains H_2O and products of drugs, toxic substances, urea, uric acid & creatinin.

Glomerular Filtration + Reabsorption + Secretion + Synthesis= Urine

GLOMERULAR FILTRATION RATE (GFR)

Definition: It is the amount of protein free plasma, which is filtered in both kidneys per minute across the glomerular membrane.

It equals 125ml/min in normal 70 kg young adult.

• It is about 10% less in females than males.

• The process of filtration is passive.

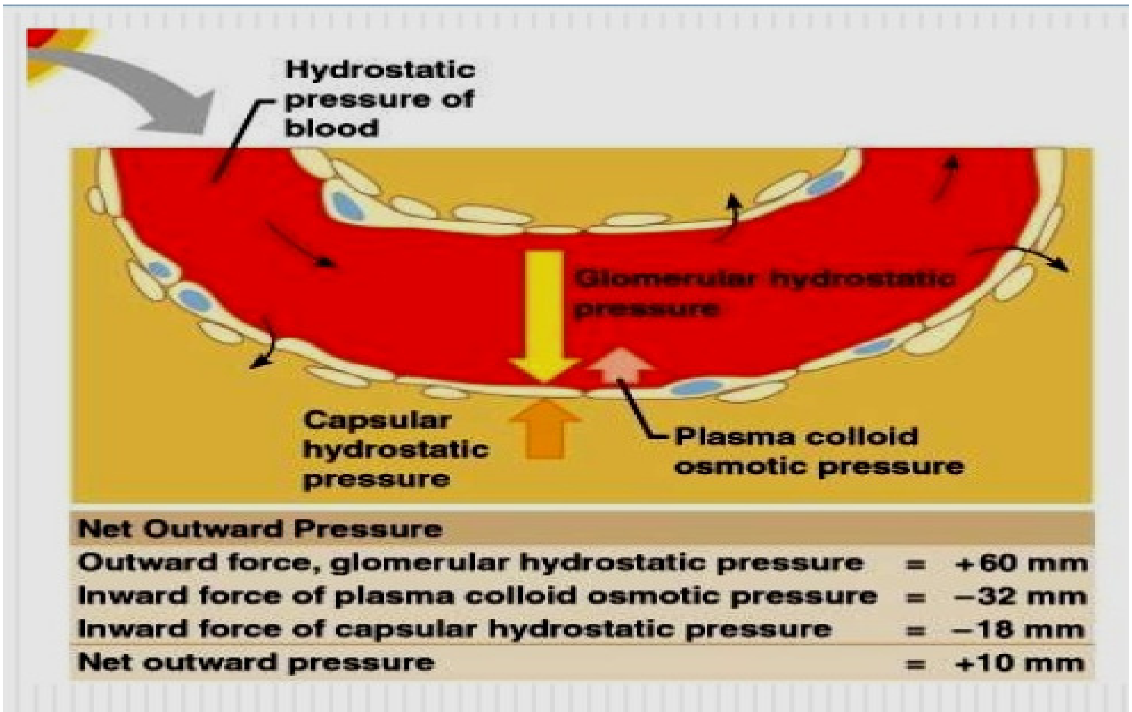
Filtration fraction: • It is the percentage of GFR as regard the renal plasma flow.

= (GFR/Renal plasma flow) x 100 = (125/700) x 100 = about 20 %

Shift of reabsorbed fluids from the interstitium to the peritubular capillaries

Starling forces or Hydrostatic forces that control fluid transport between interstitium and peritubular capillaries they are the driving forces that act across the Peritubular capillaries and control fluid transport between interstitium and peritubular capillaries.

It is determined by 4 forces:



1- <u>Forces that favor absorption</u>:

a) Colloid osmotic pressure in the peritubular capillaries

b) Hydrostatic pressure of the interstitial fluid

2<u>- Forces that oppose absorption</u>:

a) Colloid osmotic pressure of the interstitial fluid (normally = Zero).

b) Hydrostatic pressure in the peritubular capillaries

Dynamics of glomerular filtration

- Driving force for GFR is the hydrostatic pressure in glomerular capillaries = 60mm Hg.
- Opposing forces for the filtration, are:
  a) Hydrostatic pressure in Bowman's capsule = 18 mm Hg.
  b) Oncotic pressure of plasma proteins = 32 mm Hg (here it is high because high concentration of plasma proteins).

Net filtration pressure = 60 – (18 + 32) = 10 mm Hg.

Composition of the Glomerular Filtrate GF or Primary Urine: • GF composed mainly of water & freely filterable substances at equal concentrations with plasma (e.g. glucose, urea, electrolytes, amino acids,.. etc)

GF has the same properties as the plasma as regarding Its pH (7.4), specific gravity (1010) & osmolality (300 mosmol/litre).

However, it differs from the plasma in:

1. Contain small amounts of proteins (0.03 gm/dl) mainly albumin.

2. Non-protein anions (Cl^- & HCO_3^-) are 5% > plasma, while cations (Na^+ & K^+) are 5% less as a result of **Donnan equilibrium**.

Factors that affect GFR

1-Hydrostatic pressure of the glomerular capillaries = 60mm Hg.

GFR is directly proportional to glomerular capillary pressure i.e. ↑ glomerular capillary pressure → increase filtration force →increase GFR & vice versa. - This pressure is affected by diameter of afferent or efferent arterioles as:

a) An increase blood flow to the kidney (dilatation of afferent arterioles and mild constriction of efferent arterioles) will increase the glomerular capillary pressure that increases GFR.

b) Diminish renal blood flow (constriction of afferent arterioles and severe narrowing in efferent arterioles) will diminish the glomerular capillary pressure that decreases GFR.

c) Mild constriction of efferent arteriole alone could increase in the glomerular hydrostatic pressure with subsequent increase in the GFR, while severe constriction of efferent arterioles leads to decrease GFR due to diminish renal blood flow. Therefore, the relation between the diameters of both afferent and efferent arterioles greatly determines the GFR.

2-Hydrostatic pressure in Bowman's capsule = 18 mmHg.

It is the antagonizing force for filtration

• Increase Hydrostatic pressure in Bowman's capsule as by stone any obstruction in the urinary tract decreases GFR

• if maintained high leads to back pressure degeneration (hydronephrosis).

3- Oncotic pressure of plasma proteins = 32 mmHg.

• Antagonising force for filtration.

• Diminish formation plasma proteins (as in liver diseases or marked loss in kidney disease) increases GFR.

• Oncotic pressure of plasma proteins is here relatively high (32 instead of 28 mm Hg) because the filtered fluid **is protein free filtrate which increases the concentration of plasma proteins.**

4 - Permeability of glomerular membrane

It is affected by:

• Total surface area of filtration (which is determined by total number of healthy nephrons)

• State of intra-glomerular mesangial cells (contractile cells) - Mesangial contractions decrease effective filtration area with subsequent decrease in GFR . - Mesangial relaxation decrease GFR.

5 - Systemic blood pressure:

• GFR remains more or less constant between blood pressure 70 & 210 mmHg due to Auto-regulation of renal blood flow.

• Marked decrease of blood pressure below 70 mmHg as in severe haemorrhage there is marked decrease in GFR & may even stops → acute renal failure.

• Marked elevation above 210 mmHg causes an increase in GFR and urine formation phenomena called "pressure diuresis".

6 – Sympathetic stimulation: Marked sympathetic stimulation as in severe exercise or intense emotional stress diminishes GFR by constricting the renal artery

Renal Handling of Sodium

Functions of sodium in the body are:

1. Keeping volumes of both extracellular fluid & blood constant → maintains normal ABP.
2. Formation of resting membrane potential, action potential & conduction of nerve impulse.
3. Skeletal & smooth muscle contraction by releasing Ca^{++} from sarcoplasmic reticulum.
4. Controlling release of many vital substances in body as renin & Aldosterone.
5. Bone formation.

Na^+ reabsorption

- Na^+ reabsorption is ***associated with transport of many other substances*** as H_2O, H^+, glucose, amino acids, Cl^-, HCO_3^- , and K^+.

Renal handling of Na^+:

1) Na^+ reabsorption in PCT (70%).

- About 70% of Na^+ load is reabsorbed in PCT.
- **At the luminal border:** Na^+ is transported from lumen to inside cells by ***facilitated diffusion*** under effect of:

1. Concentration gradient.

2. Electrical gradient (in lumen – 3 mv & inside cell – 70 mv).

- This is helped by large surface area of brush border of PCT & by presence of carriers.

- **At baso-lateral border:** Na^+ crosses to interstitium fluid by ***active pump*** against its electrochemical gradient by Na^+- K^+ ATPase activity (for each 3 Na^+ pumped out only $2K^+$ ions are carried in).

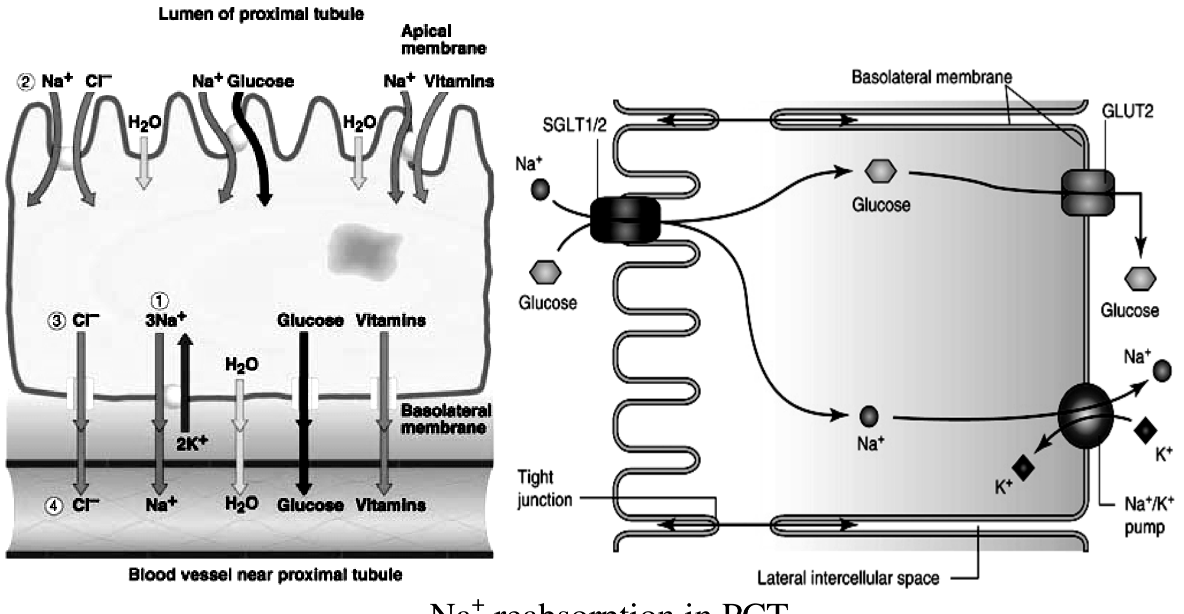
- After entering the cell *K^+ ions diffuses back again to the interstitium* helped by concentration gradient & high permeability of cell membrane → maintain the ***intracellular negativity*** in relation to luminal fluid → ↑ Na^+ entry to the cell (help the *facilitated diffusion).*

This reabsorption result in:

1- **Reabsorption of 70%** of water **"obligatory water reabsorption"** because of the high osmolality created by Na^+ reabsorption.

2- **Active co-transport transport** of glucose, amino acids, HCO_3^- & other organic acids (these substance are carried by same carrier of Na^+).

3- **Passive diffusion of Cl^-** *(in 2nd half of PCT due to ↑Cl^- concentration).*



Na^+ reabsorption in PCT

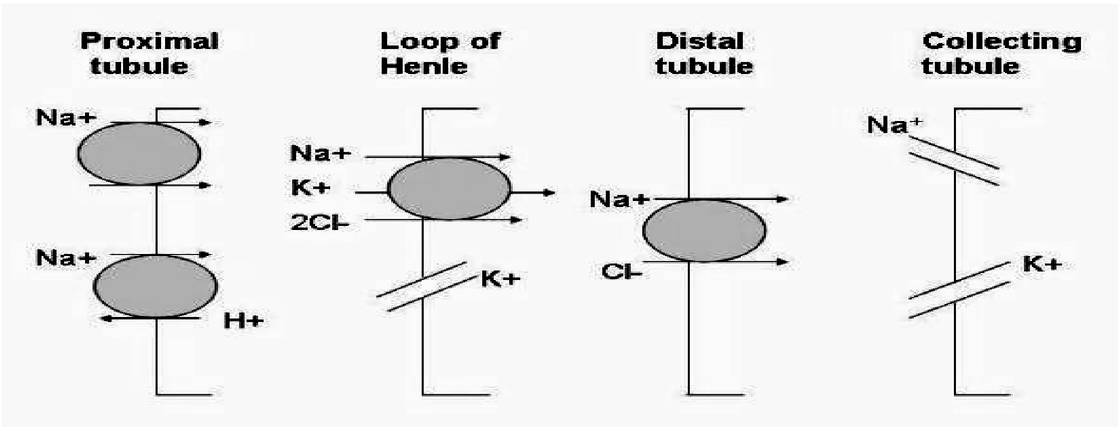
2) Na^+ reabsorption in the loop of Henle (20%)

- **Thin descending part**: ***The only part in the nephron*** in which Na^+ is not reabsorbed (also this part is freely permeable to H_2O → ***hypertonic tubular fluid***).
- **Thin ascending part:** ***passive*** reabsorption of Na^+.
- **Thick ascending part:** active reabsorbtion of **20% of Na^+** by co-transport protein carrier (1Na^+, 2 Cl^- & 1K^+) mechanism (also this part is poorly permeable to water→ fluid leaving this thick part is ***hypotonic***).

3) Na^+ reabsorption in the distal convoluting & collecting tubules (10%)

- 10% of Na^+ is ***actively reabsorbed***, in exchange with H^+ or K^+ by the help of ***Aldosterone hormone***.

NB: Na^+ reabsorption *is active along the nephron except in thin ascending part of loop of Henle.*



Na^+ reabsorption in renal tubules

Factors controlling Na^+ reabsorption:

The amount of Na+ excreted per day may be as low as 1mEq/day to as high as 400mEq/day. The factors controlling are:

1- **Amount of NaCL intake per day**: increase intake → increase Na^+ reabsorption & excretion (& vice versa).

2- **Hormonal factors:**

-Aldosterone: Acts mainly on principal cells of DCT & collecting ducts → increase Na^+ reabsorption in exchange with K^+ & H^+.

-Glucocorticoids : -Weak Aldosterone like action on sodium reabsorption → Na^+ & water retention & decrease Na^+ excretion in urine.

-Sex hormones (estrogens): Salt retention effect, so contraceptive pills that contain oestrogen → oedema in prolonged use.

-PGE₂: Increase Na^+ excretion in urine (naturesis)

- This by inhibiting Na^+ K^+, ATPase & by increase intracellular Ca^{++}, which inhibit Na^+ transport across the channels.
- Endothelins causes naturesis by increasing PGE_2.

-Atrial naturetic peptide (ANP): Decrease Na^+ reabsorption & increase excretion

3- Glomerulo-tubular balance:

- Increase GFR → increase tubular load of any substance → increase its reabsorption to prevent overloading of the distal tubules with these solutes.

4- Effect of ABP:

- Increase ABP above 180mmHg → increase Na^+ excretion & urine output “pressure diuresis”.

5- Diuretics:

- - Osmotic diuretics as mannitol→ Decrease Na+ reabsorption from PCT
- - Loop diuretics (Lasix) → Decrease Na^+ reabsorption from Henle's loop
- - Aldactone → Decrease Aldosterone → Decrease Na^+ reabsorption from DCT.

Events that occur inside PCT:

1- 70% of Na^+ load is reabsorbed.
2- 70% of water load is reabsorbed = obligatory water reabsorption .
3- Co-transport of K^+, glucose, amino acids & other organic acids at the 1st half of PCT.
4- Absorption of CL^- & secretion of H^+ ions in the 2nd half of PCT.
5- Reabsorption & synthesis of $NaHCO_3$
6- Remaining tubular fluid is **isotonic** (300mosmol) but slightly acidic ($pH<7.35$).