RENAL SYSTEM (URINARY SYSTEM)

- Urinary system consists of a pair of Kidneys, which filter blood, form urine & regulate certain metabolic processes; a pair of tubular ureters, which transport urine from kidney to bladder; a saclike urinary bladder, which stores urine, & a tubular urethra, which conveys urine to outside of the body.
- Blood enters kidney in renal artery (branch of aorta), & leaves kidney in renal vein which join the inferior vena cava.
- Composition of body fluids directly or indirectly regulated by kidney as they form urine from blood plasma.
- Although a person has 2 kidneys, 1 kidney is sufficient to carry out complex work required to maintain homeostasis of body fluids.

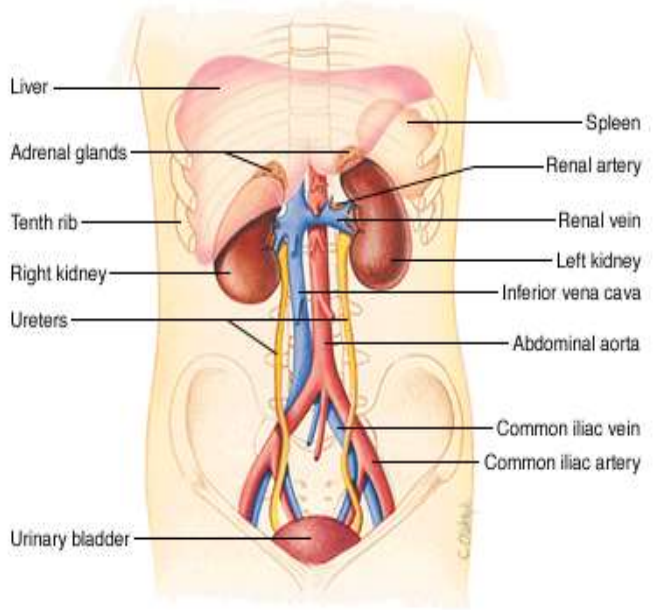
FUNCTIONS OF THE KIDNEYS;

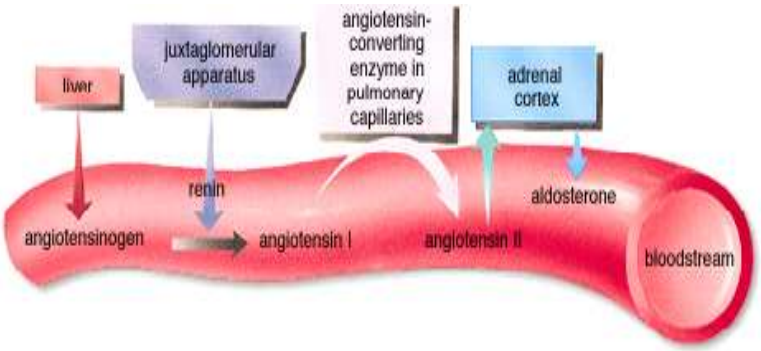
1. **Excretion** of metabolic waste products, foreign chemicals, drugs, & Hs.
2. **Regulation of Arterial blood Pressure;** kidneys contribute in:
   - ❖ long-term regulation by excreting variable amounts of Na+ &water.
   - ❖ short-term regulation by secreting vasoactive substances, such as *renin*.

Rennin angiotensin mechanism: Sequence;

- ↓BP stimulates **juxtaglomerular cells** in kidneys to secrete *renin*.
- Renin splits plasma protein *angiotensinogen*(synthesized by liver)to *angiotensin I*.
- Angiotensin I is converted to *angiotensin II* by an enzyme found in lung & vascular endothelium.
- Angiotensin II→ vasoconstriction & stimulates adrenal cortex to secrete aldosterone.

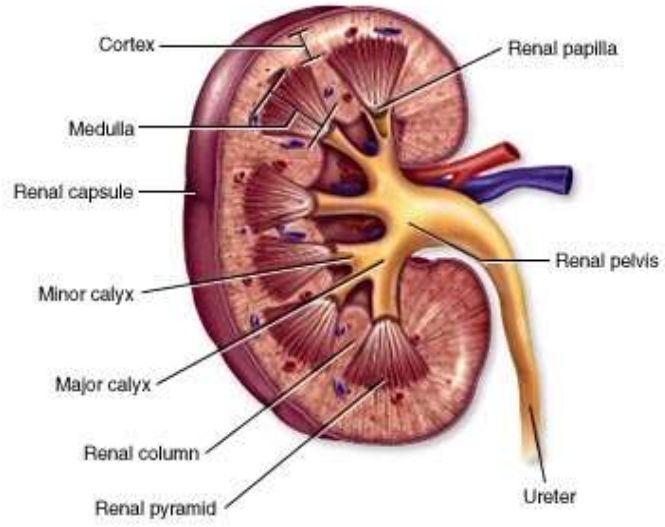
3. **Secretion of erythropoietin**—H is secreted whenever ↓blood O2 level (hypoxia).
   - ❖ It stimulates red bone marrow to ↑ the rate of RBC production.
   - ❖ Synthetic erythropoietin (Erythropoietin can be produced by genetic engineering) is available for hemodialysis patients, cancer patients & AIDS patients with severe anemia.
4. **Activation of vitamin D**—This vit. exists in several forms that are converted to calcitriol (D2) by kidney. D2 is active form of vit.D that ↑ intestinal absorption of Ca^{+2}& phosphate.
5. **Regulation of acid–base balance.**
6. **Gluconeogenesis;** kidney synthesize glucose from a.a during prolong fasting.

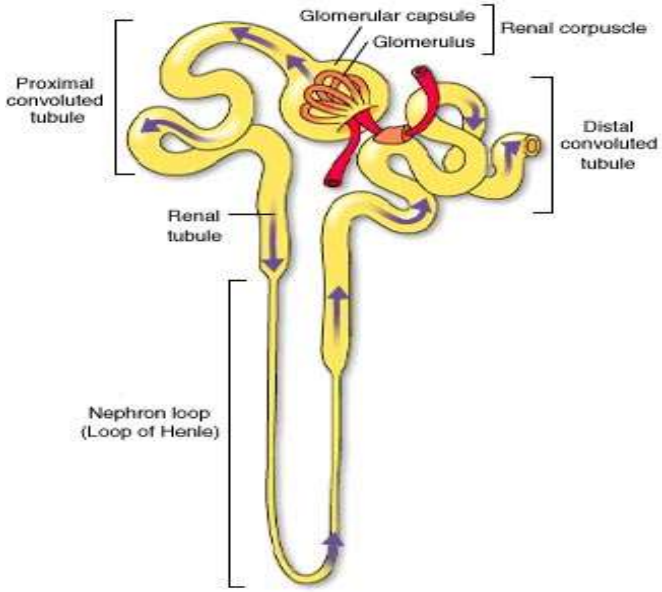




KIDNEYS:

- Kidneys are bean-shaped organs, each about the size of a tightly clenched fist.(weight 130 g).
- Renal cortex—outer layer, made of renal corpuscle & convoluted tubules.
- Renal medulla (pyramids)—inner layer, made of loops of Henle & collecting tubules.
- Renal pelvis—a cavity formed by expanded end of ureter within kidney at hilus; extensions around papillae of pyramids called *calyces*, which collect urine.





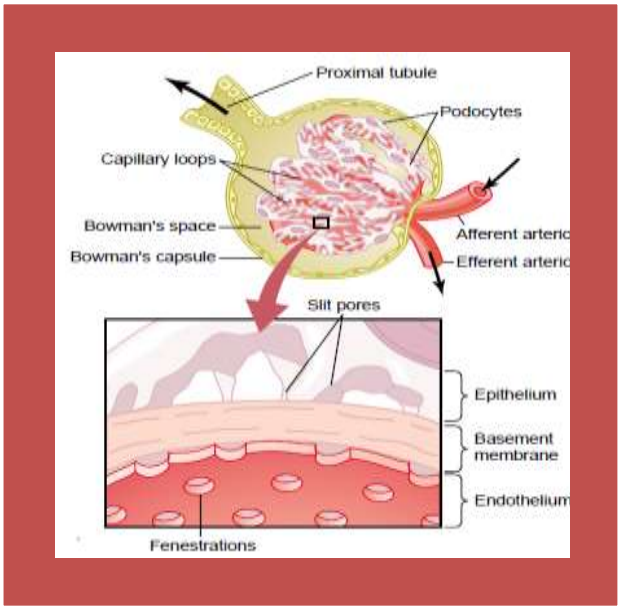
NEPHRON;

- It is structural & functional unit of kidney where urine is formed.
- Each kidney contains 1 million nephrons.
- Each nephron has two major portions: a renal corpuscle & a renal tubule.

Renal Corpuscle

☒ It consists of a glomerulus surrounded by a Bowman's capsule.

- **Bowman's capsule** is expanded end of a renal tubule; that encloses glomerulus.
  - Its Inner layer is very permeable (have pores).
  - Outer layer has no pores & is not permeable.
  - Space between inner & outer layer contains renal filtrate (fluid that is formed from blood in glomerulus & will become urine).
- **Glomerulus** is a capillary network that arises from **afferent arteriole &** empties into **efferent arteriole**. Diameter of efferent arteriole is smaller than afferent arteriole, which helps maintain a high BP in glomeruli.
- Glomerular capillary membrane has three (instead of the usual two) major layers:
  (1) *endothelium* of the capillary,
  (2) a *basement membrane.*
  (3) a layer of *epithelial cells (podocytes)*.



Renal Tubule It continues from Bowman's capsule & consists of:

- **proximal convoluted tubule- PCT** (in renal cortex),
- **loop of Henle** (or loop of nephron, in renal medulla),
- **Distal convoluted tubule-DCT** (in renal cortex).

☒ DCT from several nephrons empty into a **collecting tubule**.

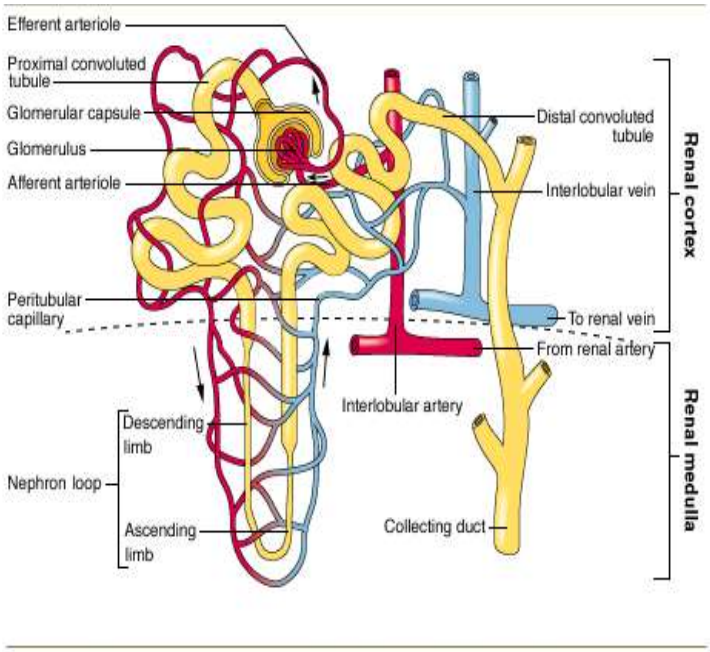
☒ Several collecting tubules unite to form a papillary duct that empties urine into a calyx of renal pelvis.

☒ Epithelial cells of collecting ducts are made of:

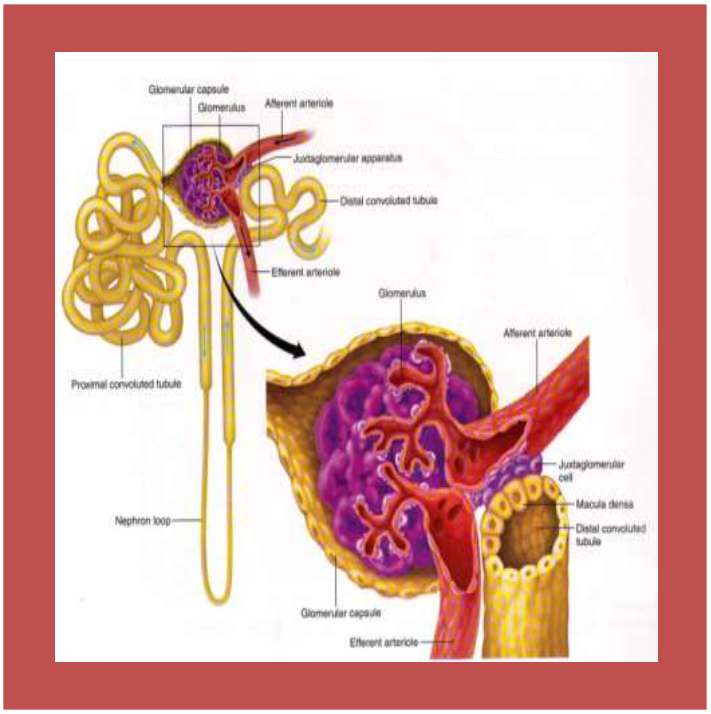
1. Principle cell (P cell) that involved in Na+ reabsorption & vasopressin stimulated H2O reabsorption,
2. Intercalated cell (I cell) that concerned with acid secretion & bicarbonate transport.

BLOOD VESSELS OF KIDNEY

- Blood flow to both kidneys is 22% of the cardiac output.
- Abdominal aorta → renal artery → small arteries in kidney →afferent arterioles →glomeruli → efferent arterioles → peritubular capillaries →small veins in kidney →renal vein →inferior vena cava.
- All parts of renal tubule are surrounded by peritubular capillaries, that receive materials reabsorbed by tubules. So, Two sets of capillaries for exchange between blood & tissues during urine formation process (glomerulus , peritubular capillaries)



Structure of a nephron and the blood vessels associated with it.



Juxtaglomerular complex consists of;

1) *Macula densa cells:*

- Specialized epithelial cells in initial portion of DCT that comes in close contact with afferent & efferent arterioles.
- Contain Golgi apparatus.

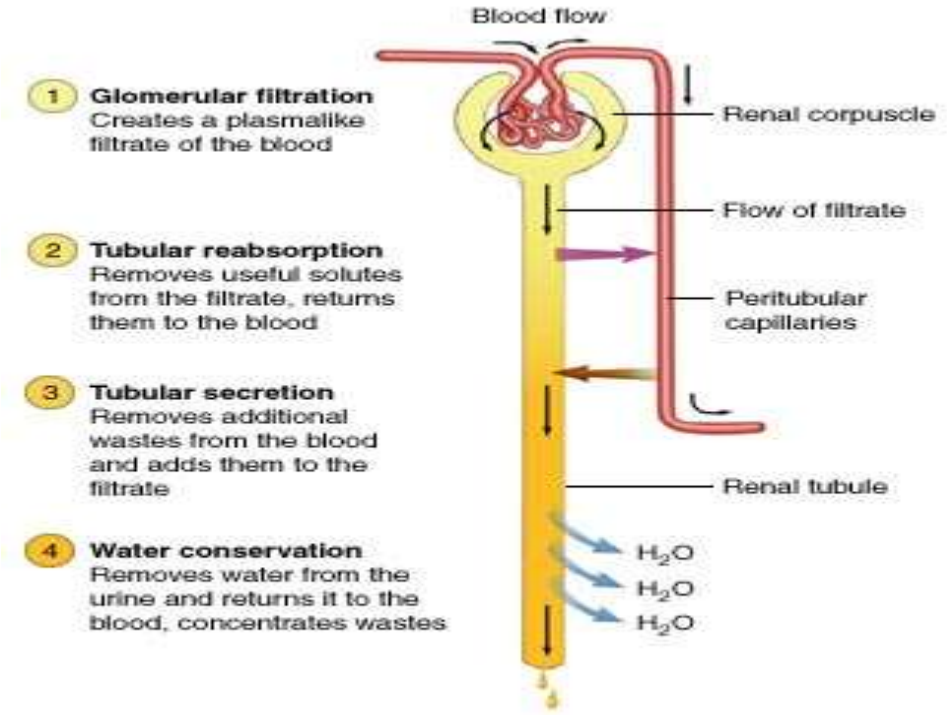
2)*Juxtaglomerular cells* in walls of afferent & efferent arterioles adjacent to macula densa.

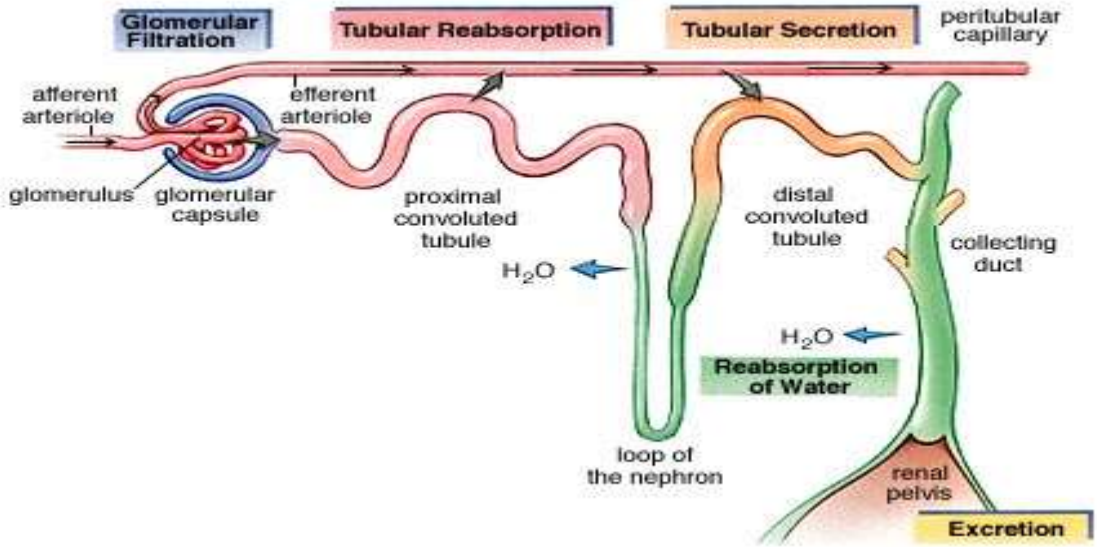
FORMATION OF URINE

It involves 3 major processes.

- ❖ Glomerular filtration, which takes place in renal corpuscles.
- ❖ Tubular reabsorption which takes place in renal tubules .
- ❖ Tubular secretion, which takes place in renal tubules.

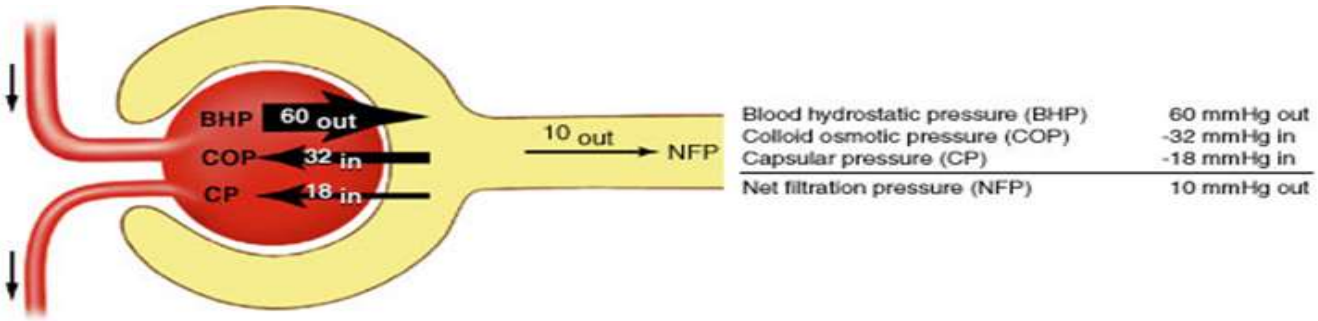
- ➢ Although about 45 gallons of filtrate is produced daily, most of water is reabsorbed (importance ?). Conservation of water is largely due to long loop of nephron, which establishes a concentration gradient in kidney tissue. Water can leave collecting duct by osmosis & return to the bloodstream in the surrounding peritubular capillaries.





GLOMERULAR FILTRATION

- Filtration is process in which BP forces plasma & dissolved material out of capillaries.
- G**lomerular filtration**, BP forces (plasma, dissolved substances, & small proteins) out of glomeruli & into Bowman's capsules. This fluid called **renal filtrate (**no longer plasma).
- ☒ BP in Glomeruli, is relatively high= 60 mmHg. & BP in Bowman's capsule is very low,
- ☒ So 20 - 25% of blood that enters glomeruli becomes renal filtrate in Bowman capsules.
- Filtration is not selective with respect to usefulness; it is selective only with respect to size. So, renal filtrate is like blood plasma, except that, less protein & no blood cells are present.
- Blood cells & larger proteins are too large, so they remain in blood.
- Waste product & useful material (e.g nutrient, mineral) dissolved in blood plasma→ pass into filtrate.
- **Net Filtration Pressure**
  Filtration pressure across filtration membrane is equal to blood hydrostatic pressure (BHP) minus colloid osmotic pressure (COP) in glomerular capillary &minus capsular pressure (CP).



Glomerular filtration rate (GFR) is amount of renal filtrate formed by kidneys in 1 min. it equals to (100 - 125 mL / min).

❖ Factors Affecting GFR.

- Changes in renal blood flow.
  - ↑ blood flow→ ↑ GFR, & more filtrate is formed.
  - ↓ blood flow→↓ GFR(severe hemorrhage), less filtrate is formed, & ↓ urinary output.
- Changes in hydrostatic pressure of glomerular capillaries .
- Changes in hydrostatic pressure of Bowman's capsule.
- Changes in systemic BP.
- Afferent or efferent arteriolar constriction.
- Ureteral obstruction
- Changes in concentration of plasma proteins : dehydration, hypoproteinemia. (minor effect)

Measurement of GFR: it can be measured by calculating the clearance of a substance. Clearance: it is volume of blood cleared of a substance per unit of time. The substance criteria (as Inulin substance);

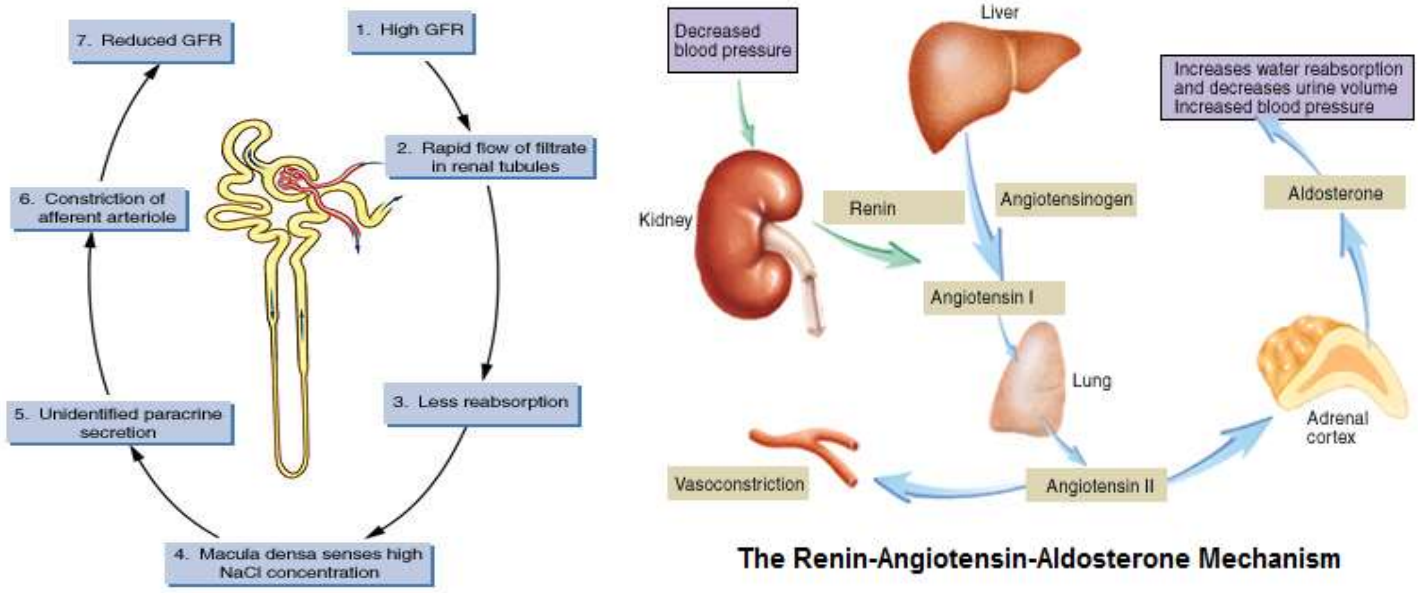
- Freely filtered.
- Not toxic & not affecting GFR.
- Not metabolized or stored in kidney.

$$\text{Inulin clearance in urine (mg/dl)} = \frac{\text{urine volume ml per min X conc. Of inulin}}{\text{plasma inulin conc. mg/dl}}$$

Autoregulation of Glomerular Filtration Rate (GFR)

GFR must be precisely controlled. The kidneys are able to maintain a relatively stable GFR in spite of changes in blood pressure; however, it is not able to compensate for extreme blood pressure variations.

Juxtaglomeriolar apparatus monitor BP. Rennin is released in response to ↓ BP → a complex chain of reactions is initiated by the release of rennin.angiotensin II causes adrenal cortex to release aldosterone → ↑ tubular reabsorption of Na+ which causes ↑ water reabsorption → ↑ blood volume & thus BP.



The Renin-Angiotensin-Aldosterone Mechanism

TUBULAR REABSORPTION

It takes place from filtrate in renal tubule to blood in peritubular capillaries.

- In a 24-hr period;
  - Kidneys form 150-180 L of filtrate,
  - Normal urinary output is 1-2 L.
  - 99% of filtrate is reabsorbed back into blood of peritubular capillaries.
  - 1% of filtrate enter renal pelvis as urine.
- Most reabsorption & secretion (65%) take place in PCT.
- DCT & collecting tubules are also important sites for reabsorption of water.

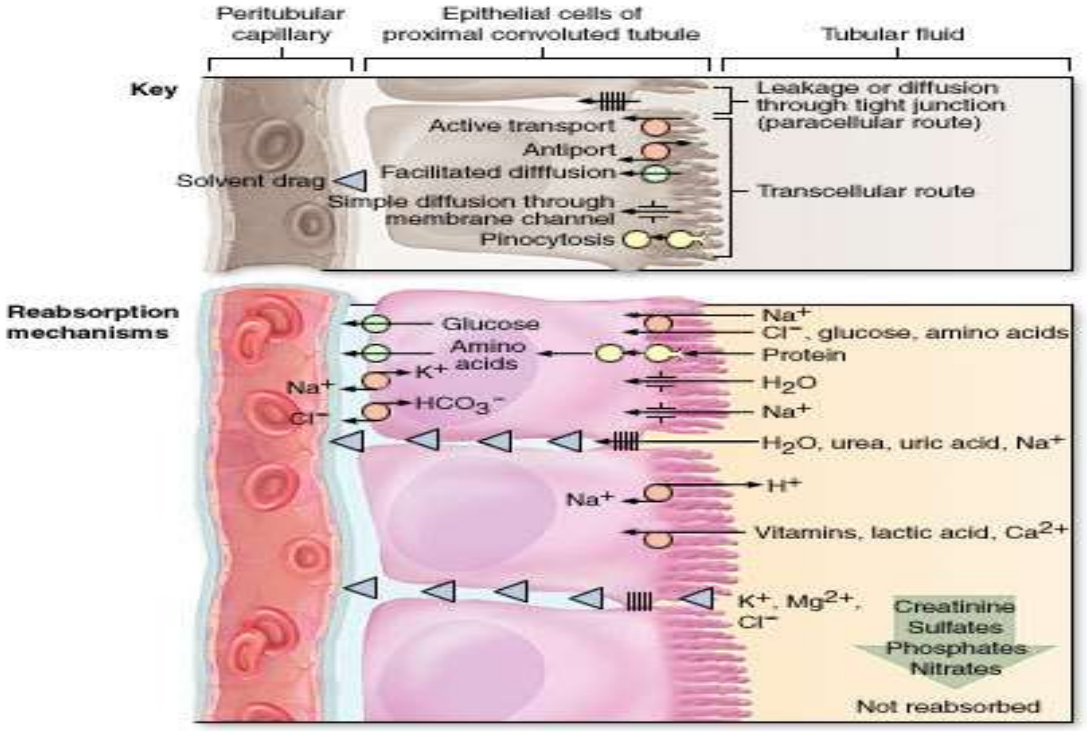
Mechanisms of Reabsorption

1) Active transport—reabsorption of glucose, a.a, vitamins, & +ve ions; in which threshold level is limited to quantity that can be reabsorbed. Example;
   - If filtrate level of glucose is normal & number of glucose transporter molecules in membranes of tubules is sufficient. So, tubules will reabsorb all of glucose, & no glucose will be found in urine.
   - If, blood glucose is above normal, amount of glucose in filtrate will also be above normal & will exceed threshold level of reabsorption. Glucose molecules is more than number of transporter molecules available→ some glucose remain in filtrate & present in urine.
2) Passive transport—most - ve ions follow reabsorption of +ve ions.
3) Osmosis—water follows the reabsorption of minerals, especially Na.
4) Pinocytosis— small proteins are large to be reabsorbed by active transport →they engulfed by PCT.

TUBULAR SECRETION

Substances are actively secreted from blood in peritubular capillaries into filtrate in tubules.

- Waste products, such as ammonia & creatinine, & metabolic products of medications.
- Hydrogen ions (H+) may be secreted by tubule cells to help maintain normal pH of blood.



HORMONES THAT INFLUENCE REABSORPTION OF WATER

Antidiuretic hormone (ADH) ; from pituitary gland:

- ↑reabsorption of water from the filtrate to blood.

Parathyroid hormone (PTH); from parathyroid gland:

- ↑ reabsorption of Ca+2 ions from filtrate to blood & excretion of phosphate ions into the filtrate.

Aldosterone hormone ; from adrenal gland:

- ↑ Reabsorption of Na+ ions from filtrate to blood & excretion of K+ ions into the filtrate. Water is reabsorbed following reabsorption of Na+.

Atrial natriuretic peptide (ANP) (atria of heart)

- ↓ reabsorption of Na+ ion, which remain in filtrate. More Na+ & H2O are eliminated in urine.

Role of ADH in Regulating Urine Concentration and Volume
1. Concentration of water in blood decreases.
2. Increase in osmotic pressure of body fluids stimulates osmoreceptors in hypothalamus in brain.
3. Hypothalamus signals posterior pituitary to release ADH.
4. Blood carries ADH to kidneys.
5. ADH causes distal convoluted tubules and collecting ducts to increase water reabsorption.
6. Urine concentrates, and urine volume decreases.

Urine Concentration:

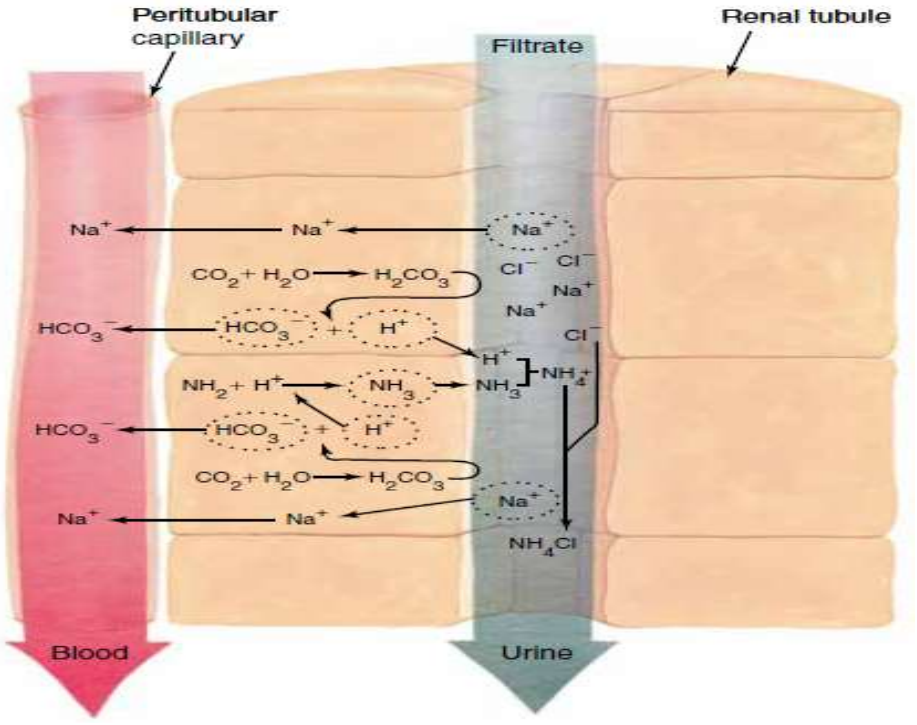
1- More salt is continually added by the PCT.
2- The higher the osmolarity of ECF, the more water leaves the descending limb by osmosis.
3- The more water that leaves the descending limb, the saltier the fluid that remains in the tubule.
4- The saltier the fluid in the ascending limb, the more salt the tubule pumps into ECF.
5- The more salt that is pumped out of ascending limb, the saltier the ECF is in the renal medulla.

THE KIDNEYS AND ACID–BASE BALANCE

- Kidneys are the organs that are most responsible for maintaining pH of blood & tissue fluid within normal ranges.

If body fluids become too acidic	If body fluids become too alkaline
- Kidneys excrete H^- ions - Return $HCO3^-$ ions to blood.	- Kidneys return H^- ions to blood. - Excrete $HCO3^-$ ions.

- Renal tubules secrete H+ ions or ammonia in exchange for Na+ ions → influence reabsorption of other ions.
- H+ ions are obtained from reaction of CO2 & H2O.
- Amine group (NH2) from a.a is combined with H+ ion to form ammonia (NH3).
- Tubule cell secretes H+ ion & ammonia into renal filtrate, & 2 Na_ ions are reabsorbed in exchange.
- In the filtrate, H+ ion + NH3→ NH4 _ , which reacts with Cl- to form NH4Cl (ammonium chloride) that is excreted in urine.
- As Na_ ions are returned to blood in peritubular capillaries, HCO3- ions follow.
- **Notice**: 2 H+ ions excreted in urine, & 2 Na+ ions & 2 HCO3- ions returned to blood.
- Another mechanism used by cells of kidney tubules to regulate pH is phosphate buffer system.



ELIMINATION OF URINE

Ureters, urinary bladder, & urethra do not change composition or amount of urine.

URETERS

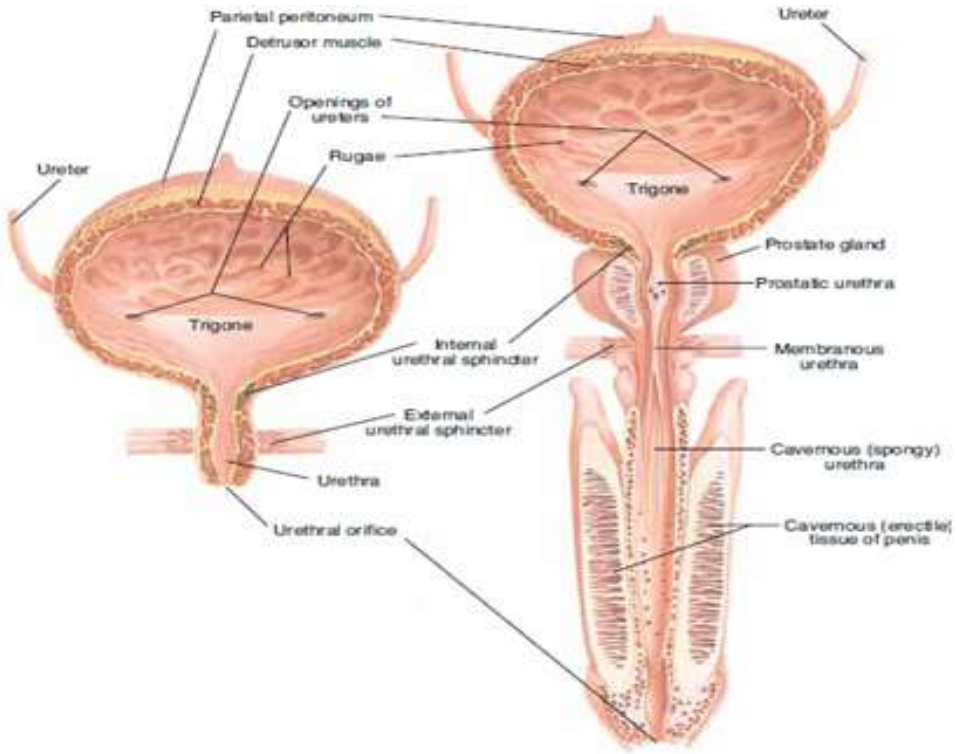
Smooth muscle in uretric wall contracts in peristaltic wave to propel urine toward bladder. As bladder fills, it expands & compresses lower ends of ureter to prevent back flow of urine.

URINARY BLADDER

- It is a muscular sac that reserve accumulating urine, & it contracts to eliminate urine.
- *Mucosa*—transitional epithelial tissue folded into rugae; permit expansion without tearing.
- Trigone—triangular area on bladder floor; no rugae, does not expand; bounded by openings of ureters & urethra.
- Detrusor muscle—smooth muscle layer, a spherical; contracts to expel urine (reflex).
- Internal urethral sphincter—involuntary; formed by detrusor muscle around opening of urethra.

URETHRA

- It carries urine from bladder to the exterior.
- External urethral sphincter**,** voluntary **,** made of surrounding skeletal muscle of pelvic floor.



THE URINATION REFLEX **(micturition** or **voiding**).

- This reflex is a spinal cord reflex over which voluntary control may be exerted.
- Stimulus for reflex is stretching of detrusor muscle of bladder.
- Bladder can hold 800 mL of urine, but reflex is activated long before maximum is reached.

❖ When urine volume reaches 200 - 400 mL, stretching generate sensory impulses to→ sacral spinal cord→ Motor impulses return along parasymp. nerves to detrusor m.→ contraction.

❖ At the same time, internal urethral sphincter relaxes.

- If external urethral sphincter is voluntarily relaxed, urine flows into urethra, & bladder is emptied.
- If bladder continues to fill & be stretched, voluntary control is no longer possible.

CHARACTERISTICS OF URINE (urinalysis)

Amount: 1–2 L / 24 hrs; variable depending on fluid intake & water loss through skin & GI tract;
Color—typical yellow color of urine (from urochrome, a breakdown product of bile).
Specific gravity- (1.010 - 1.025); this is a measure of dissolved materials in urine.

- ❖ Specific gravity of distilled water is 1.000, means that there are no solutes present. So, the higher the specific gravity number, the more dissolved material is present.
- ❖ Strenuous exercise & sweating produce less urine→ more concentrated & higher specific gravity.

pH—(4.6 - 8.0, with an average value of 6.0). Diet has the greatest influence on urine pH .

- A vegetarian diet → more alkaline urine. • High-protein diet → more acidic urine.

Constituents—urine is 95% H2O, which is the solvent for waste products & salts. Salts are not considered true waste products because they may well be utilized by the body when needed.
Nitrogenous wastes— all of these wastes contain nitrogen.

- ❖ Urea is formed by liver, when excess a.a are deaminated to be used for energy production.
- ❖ Creatinine from metabolism of creatine phosphate, (an energy source in muscles).
- ❖ Uric acid from metabolism of nucleic acids, that is, breakdown of DNA & RNA.
- ➢ Although these are waste products, there is always a certain amount of each in blood.

Other ***non-nitrogenous waste*** products include;

- ❖ Small amounts of urobilin from Hb of old RBCs,
- ❖ Metabolic products of medications.

AGING AND THE URINARY SYSTEM

- ❖ Number of nephrons ↓, often to half the original number by age of 70 – 80.
- ❖ Kidneys lose some of their concentrating ability.
- ❖ ↓GFR, partly as a consequence of arteriosclerosis & diminished renal blood flow.

➢ Despite these changes, excretion of nitrogenous wastes remains adequate.

- ❖ ↓Urinary bladder size & ↓detrusor muscle tone.

➢ These changes may lead to a need to urinate more frequently.
✓ ***Hemodialysis*** is the use of an artificial kidney machine. Patient's blood passes through minute tubes surrounded by fluid with the same chemical composition as plasma.
✓ **Osmotic pressure** of the solution is the pressure necessary to prevent solvent migration.
✓ **Oncotic pressure**:colloid osmotic pressure due to plasma colloids **(**plasma protein & other colloids**).**
✓ **Hydrostatic pressure**— by the weight of blood itself in blood vessels.

Control of the micturation reflex by higher brain centers

A. Ascending pathways carry an increased frequency of action potentials up the spinal cord to the brain when the urinary bladder becomes stretched.

B. Descending pathways carry action potentials to the sacral region of the spinal cord to inhibit the micturation reflex tonically and to stimulate the reflex when stretch of the urinary bladder produces the conscious urge to urinate and when one voluntarily chooses to urinate.

Micturation reflex

1. Urine in the urinary bladder stretches the bladder wall.
2. Action potentials produced by the stretch receptors (blue line) are carried along pelvic nerves to the sacral region of the spinal cord.
3. Action potentials are carried by the parasympathetic nerves (black line) to relax the internal urinary sphincter and to contract the smooth muscles of the urinary bladder. Decreased action potentials carried by the somatic motor nerves (green line) cause the external urinary sphincter to relax.