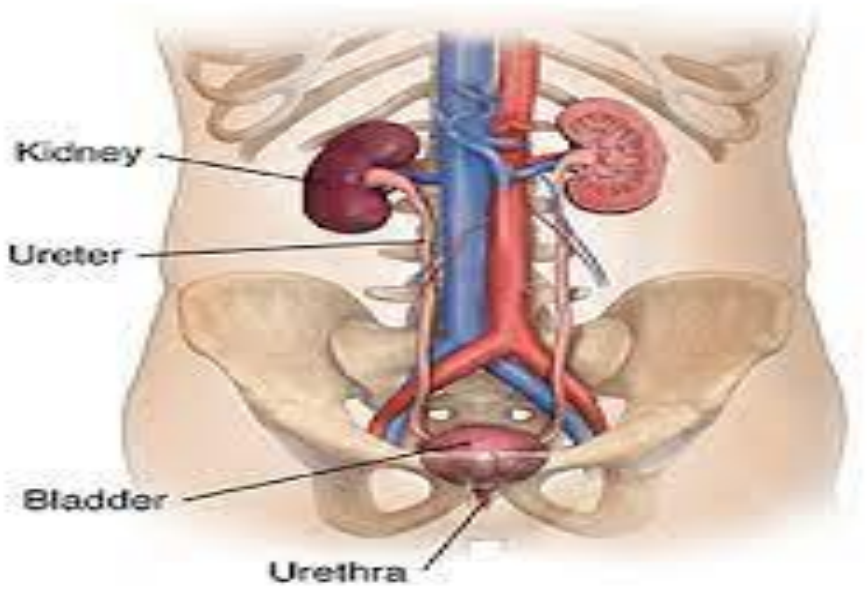
URS MODULE

Urinary system



Objectives

- ***Demonstrate** the gross anatomy of the kidney.*
- ***Demonstrate** the gross anatomy of Ureters and urinary bladder.*
- ***Discover** The gross anatomy of urethra*
- ***Illustrate** The microscopic picture of the kidney*
- ***Illustrate** The microscopic picture of juxta glomerular apparatus*
- ***Illustrate** The microscopic picture of urinary blabber , ureters*
- ***Describe** Physiologic structure of the nephron of the kidney, types of nephrons, formation of urine and renal blood and plasma flow*
- ***Describe** Glomerular filtration rate and reabsorption of sodium, potassium and glucose and diuretics*
- ***Describe** Function of the different tubular segments and reabsorption of water and concentration of urine*
- ***Describe** Renal handling of glucose and sodium*
- ***Describe** Mechanism of urine concentration*
- ***Describe** Counter current mechanism*
- ***Describe** Acid base balance*

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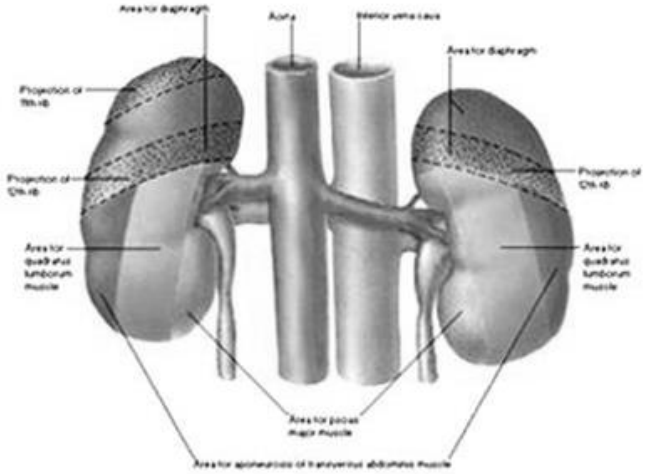
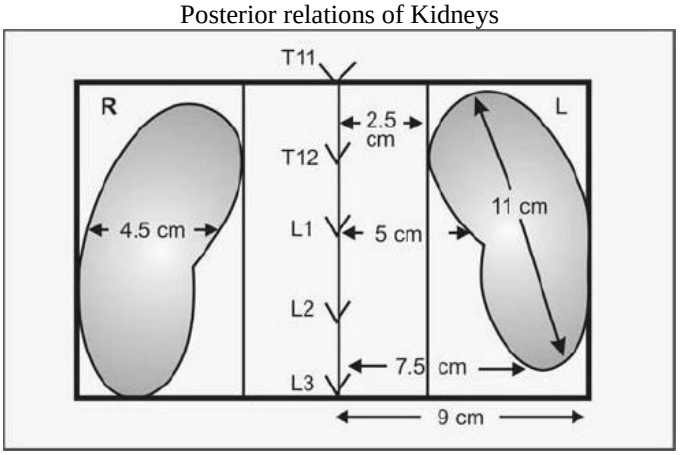
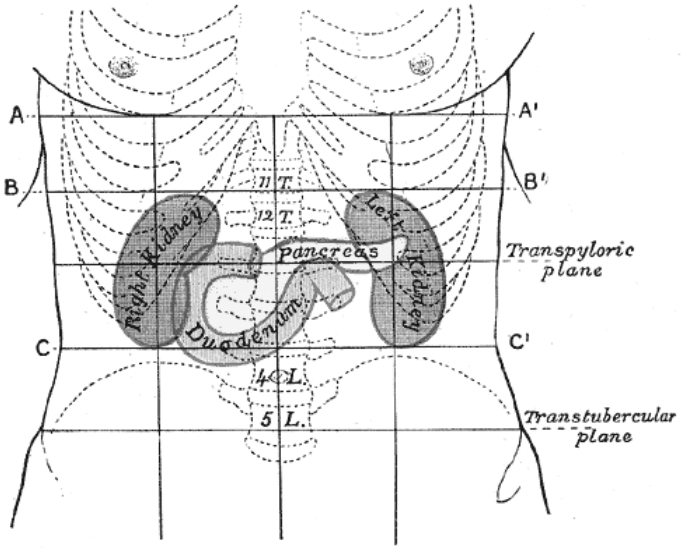


Posterior relations of Kidneys



Surface anatomy of kidney (post)



Surface anatomy of kidney (ant)

KIDNEYS

❖ 2 retroperitoneal organs. Develops in the pelvis and ascends to the abdomen. The Rt is lower than the Lt (by 0.5 inch) as the liver prevents its further ascend.

Size: 12x6x3cm (4x2x1 inches)

Shape and relations: pean shaped, has 2 surfaces, 2 borders and 2 ends.

	Rt	Lt
Upper end	Broad & near the midline	
Lower end	Thin and far from midline	
Lat border	Convex	
Med border	Concave, shows the hilum which contains renal V, renal A & ureter (from ant to post):	
Post relations:		
Upper ⅓	Diaphragm (separating it from lung, pleura & 12th rib)	Diaphragm (separating it from lung, pleura & 11th & 12th ribs)
Lower ⅔		
From med to lat	• Psoas major	• Quadratus lumborum • Transversus abdominis
Separated from Ms by	• Subcostal N & vessels	• Iliohypogastric N • Ilioinguinal N
Ant relations		
Superomedial	Rt suprarenal gland	Lt suprarenal gland
Inferomedial	• Small intestines • Ascending branch of Rt colic	• Small intestines • Ascending branch of sup Lt colic
Inferolateral	Rt colic flexure	Descending colon
Superolateral		Spleen
Ant surface	• Duodenum (2nd part): ant to hilum • Liver (Rt lobe)	• Splenicorenal ligament (containing tail of pancreas & splenic vessels): crossing the hilum to the spleen • Stomach (between suprarenal, spleen & pancreas)
Surface anatomy:		
Post (Morris rectangle)	2 horizontal lines at T11 & L3 spines 2 vertical lines 1 & 3 inches from midline	
Ant		
Upper end	11th intercostal space 1 inch from midline	11th rib 1 inch from midline
Lower end	2.5 inches above iliac crest, 3 inches from midline	2 inches above iliac crest, 3 inches from midline
Hilum	Just below L1, 2 inches from midline	Just above L1, 2 inches from midline
N.B.:	Levels are during expiration, during inspiration the kidneys descend by 1 inch	
Peritoneal coverings:	Areas related to liver & small intestines	Areas related to stomach, spleen & small intestines

Coverings of the kidney: (from inside outwards)

1) **True fibrous capsule:** fixed to the cortex & lines the renal sinus.

2) **Perirenal fat** (fatty capsule).

3) **Perirenal fascia** (Zuckerkandl fascia, false capsule).

— Part of fascia transversalis, splits into 2 layers (ant & post)

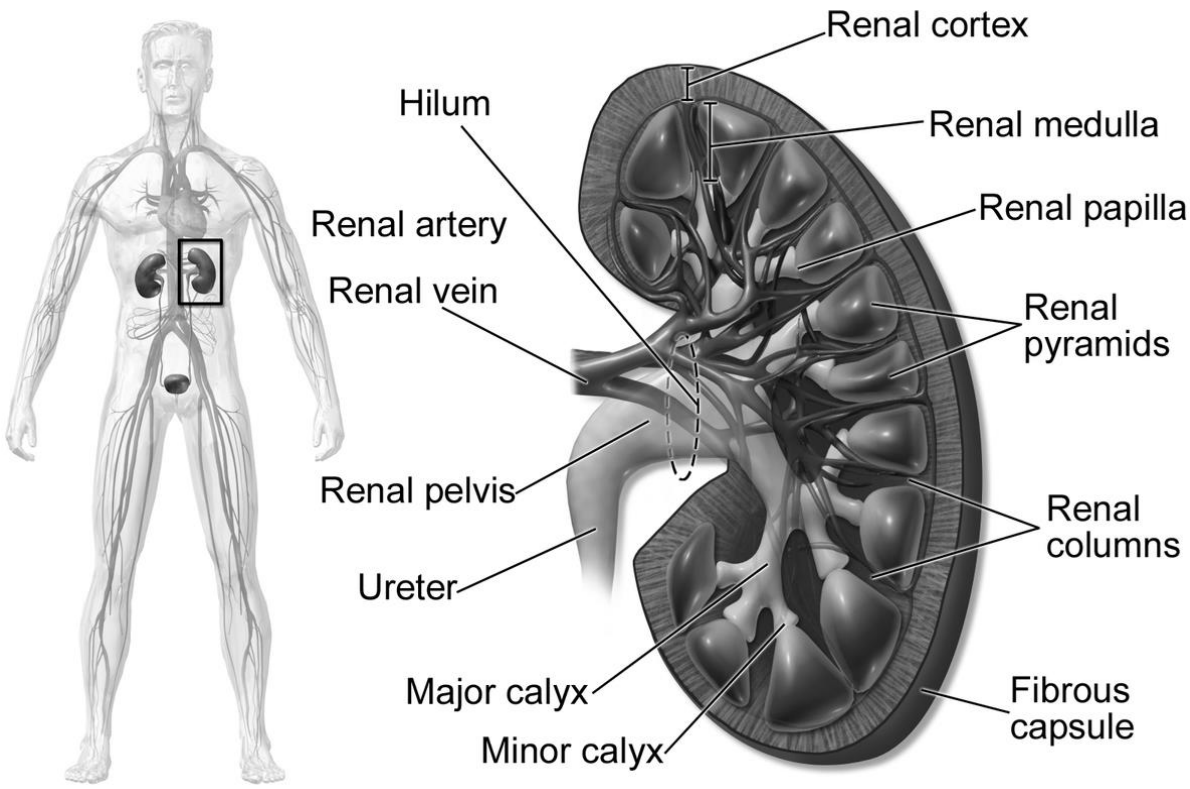
— Surrounds the kidney & suprarenal gland.

— Fuses together at the sup & lat aspects of kidney but separated at med & inf.

— The post layer is attached to the vertebral column.

— the ant layer is attached to IVC on the Rt side and aorta on the Lt side.

4) **Pararenal fat.**



Internal structure of kidney

Internal structure of kidney: formed of outer cortex and inner medulla. The unit of filtration is the nephron, it secretes urine in a collecting duct → minor calyces (8-12/ kidney) → major calyces (2-4/ kidney) → pelvis → ureter.

Support of the kidney:

- Renal vessels.
- Coverings (fat & fascia).

Blood supply:

Arterial: ***renal A*** (of aorta):

— It gives 4-6 branches at the hilum → lobar As → interlobar As (end art)

— Accessory renal A: occasional A, pierces one of the ends.

Veins: ***renal vein***

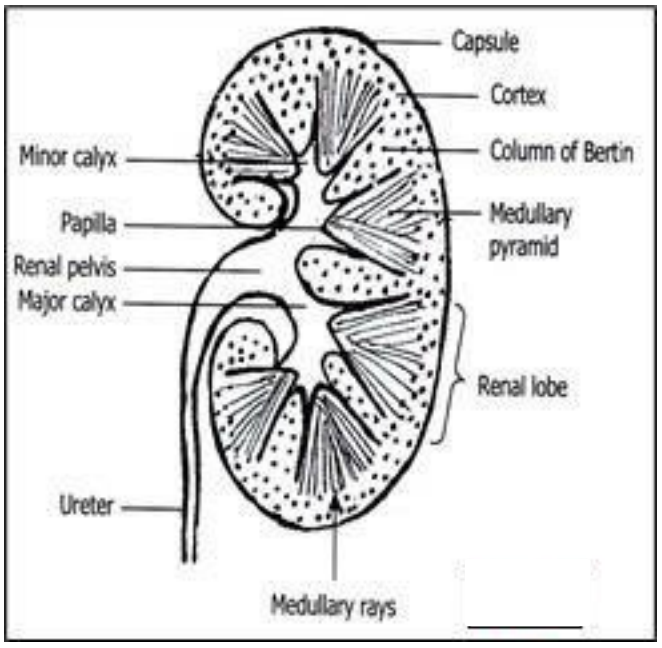
— It drains into IVC

— The Lt renal V receives Lt gonadal and Lt suprarenal Vs.

Nerve supply: renal plexus (autonomic). It communicates with testicular plexus (referred pain to the testis).

❖ Histology of Kidney: (Fig.8)

1-Capsule
2-Cortex
3-Medulla
4-Extra-renal passages



1-Capsule: Thin, formed of dense collagen fibers + Elastic fibers + Smooth ms.

2-Cortex: Broad outer zone of kidney (Dark brown and granular).

- **Subdivisions:**

Cortical arch: Between the capsule and base of medullary pyramids.
Columns of Bertini: Between renal pyramids.
Labyrinth: Convoluted tubules around medullary rays.

- **Structures present in Cortex:**

Renal corpuscles, Convoluted tubules, loop of Henle and collecting ducts.

3-Medulla: Deep to cortex

- **Subdivisions:**

Renal pyramids: 6: 12 Inverted cones:
Bases are adjacent to the cortex.
Apex called Renal papilla and fitting int minor calyces.

Each pyramid contains:
Collecting tubules (rays).
Loops of Henle.
Vasa recta (Straight blood vessels).

Medullary rays: Stripes of medullary tissue extending into the cortex
(Rays represent loop of Henle, vasa recta & collecting tubules).

Renal lobulations

- **Renal lobe:**

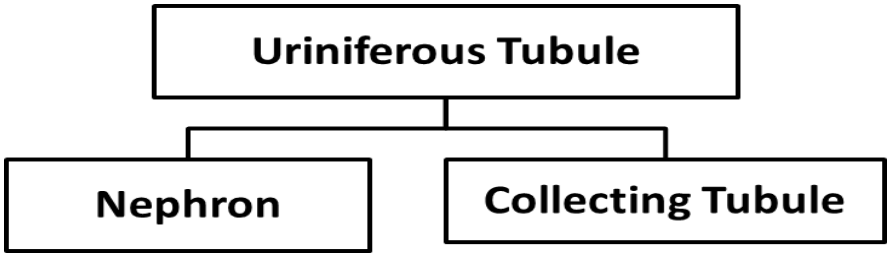
A medullary pyramid + the surrounding columns of Bertini + the overlying cortical arch.

Renal lobes are demarcated by inter-lobar vessels.

- **Renal lobule:**

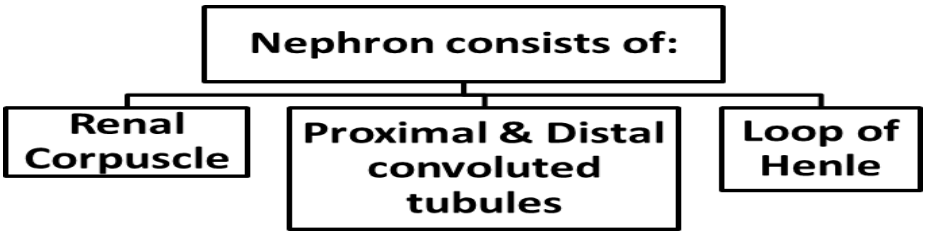
A central medullary ray and the adjacent cortical labyrinth.

Renal lobules are demarcated by inter-lobular vessels.



- **The Nephron (The functional part):**

1.5 : 2 million per kidney (**Fig.9**).



Types:

1-Cortical nephrons: With short loop of Henle.

2-Juxta-medullary nephrons: With long loop of Henle.

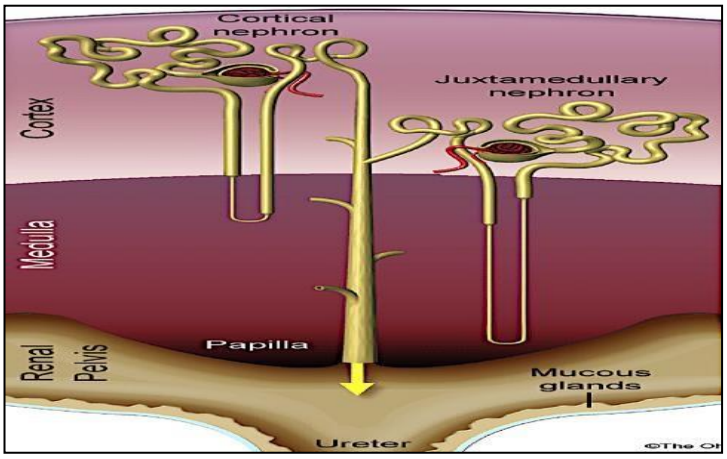


Fig.9

1-Renal corpuscle: round structures in cortex 200: 250 µm in diameter (**Fig.10**).

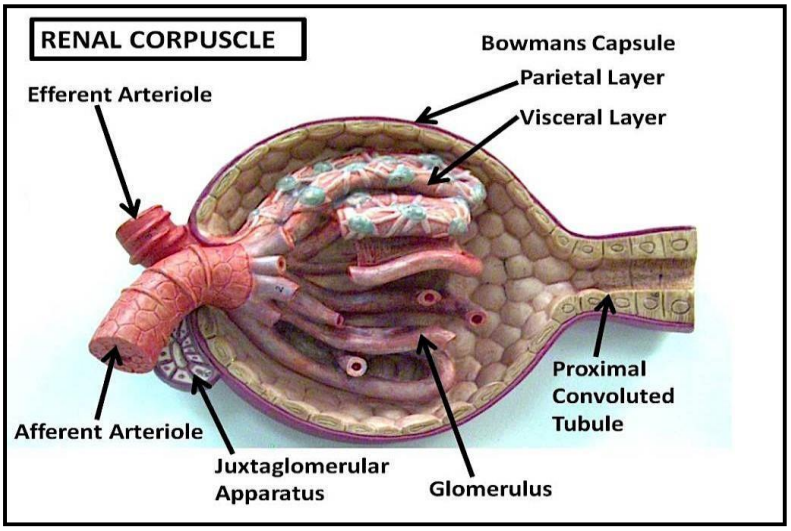


Fig.10

Components (Fig. 11):

A- Glomerulus:

- A tuft of fenestrated capillaries [whose pores lack diaphragms] to filter blood
- Formed by an afferent arteriole and drains into efferent arteriole.
- Intraglomerular mesangial cells: Pericyte-like cells between glomerular capillaries

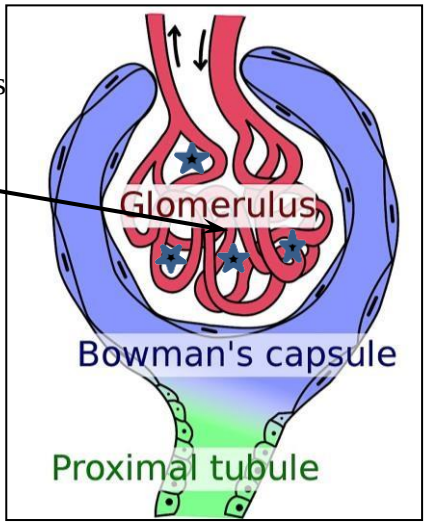


Fig.11

Function of mesangial cells:

1- Phagocytosis of foreign bodies
2- Physical support of glomerular capillaries
3- Share in renewal of glomerular basement membrane

B-Bowman's capsule:

Poles of Bowman's capsule:

a- Vascular pole: Where afferent and efferent arterioles enter and leave the renal corpuscle, respectively

b-Urinary pole: Where the parietal layer of Bowman's capsule is continuous with the proximal convoluted tubule

Structure of Bowman's capsule (Fig.12):

-Double-walled epithelial capsule

-With central space called **Bowman's space** surrounding the glomerulus to receive the fluid filtered from blood.

-Has two layers:

a- Parietal (Outer) layer: Simple squamous epithelium

b- Visceral (Inner) layer:

Formed of Podocytes (**fig. 12).**

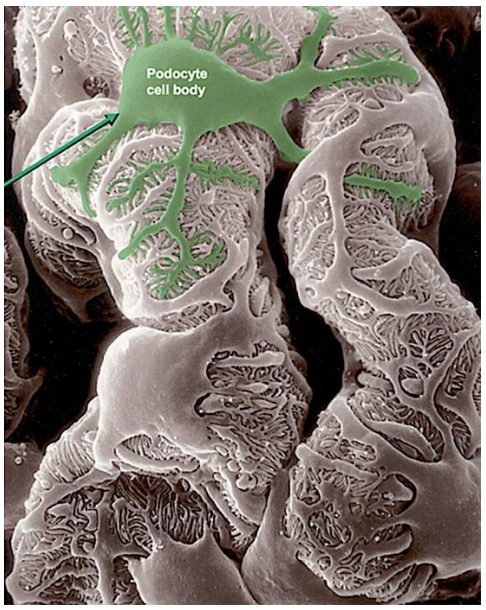


Fig. 12

Podocytes

- Define: (Fig. 13)

- Modified squamous cells forming the visceral layer of Bowman's capsule.
- Has cell body with irregular nucleus, rER, Golgi App. and numerous ribosomes.
- Cell body sends long cytoplasmic extension called primary process, which sends many secondary processes.
- Terminate by feet processes firmly implanted on glomerular basement membrane.
- The spaces between feet processes (Filtration slits) are covered by slit diaphragm.
- Podocytes are separated from glomerular basement membrane by sub-podocytic space.

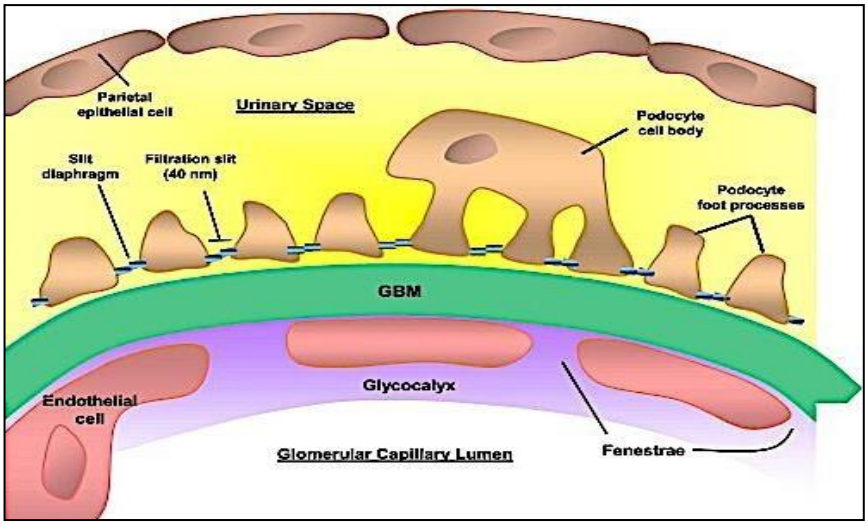


Fig. 13

- Function of Podocytes:

1- A component in renal blood barrier which restrict passage of plasma albumin and globulin.

2- Regulation of glomerular filtration rate: Contraction of podocytes → Closure of filtration slits → Reduce surface area for filtration.

3-Secretion and maintenance of glomerular basement membrane material.

Renal Blood Barrier [Filtration barrier]

- Define: Barrier between blood in glomerular capillary and space of Bowman's capsule (**Figs. 13,14**).

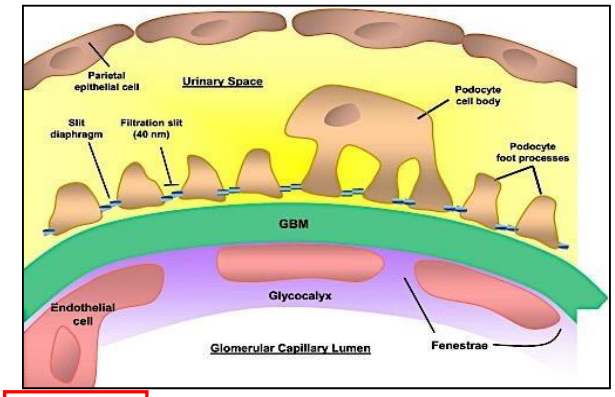


Fig. 13

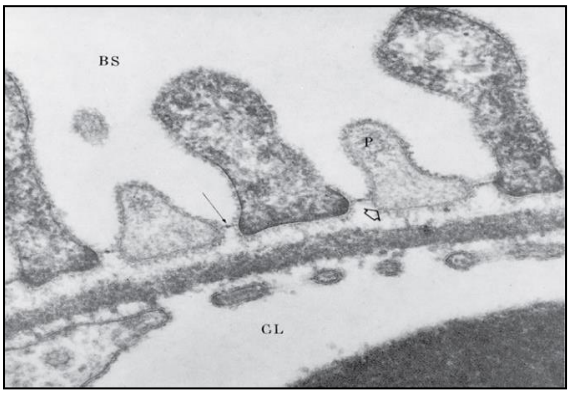


Fig. 14

- Structure:

1- Glomerular endothelium of glomerular capillary:

- Fenestrated [Has pores measuring 70:90 nm], not covered by diaphragm.
- Prevent filtration of RBCs, WBCs & platelets.
- Allow filtration of water, salts & plasma proteins.

2- Glomerular basement membrane:

- Fused basal laminae of both overlying podocytes and underlying glomerular endothelium.

-Thick and continuously renewed & it is the most important component of renal barrier.

-By E/M: Formed of 3 layers **(Fig.14)**:

Lamina densa: Middle dark layer, formed of Type IV collagen and laminin.

2 Lamina rara (Interna and externa): Pale outer and inner layers, formed of heparan sulfate.

- Prevent filtration of macromolecules.
- Prevents (Plasma albumin and globulin) by repulsion of its negative charge.
- Allow filtration of micro-molecules (water, glucose, and ionic salts).

3- Slit diaphragms between feet processes of podocytes

- Formed of cell-surface proteins (Nephrin and P-cadherin protein).
- Allow filtration of micro-molecules (water, glucose, and ionic salts).

Renal tubules

- The journey of urine starts as glomerular filtrate of the blood in Bowman's space then continues into the renal tubules in the following order **(Fig.15)**:

1- Proximal convoluted tubule.
2- Loop of Henle.
3- Distal convoluted tubule.

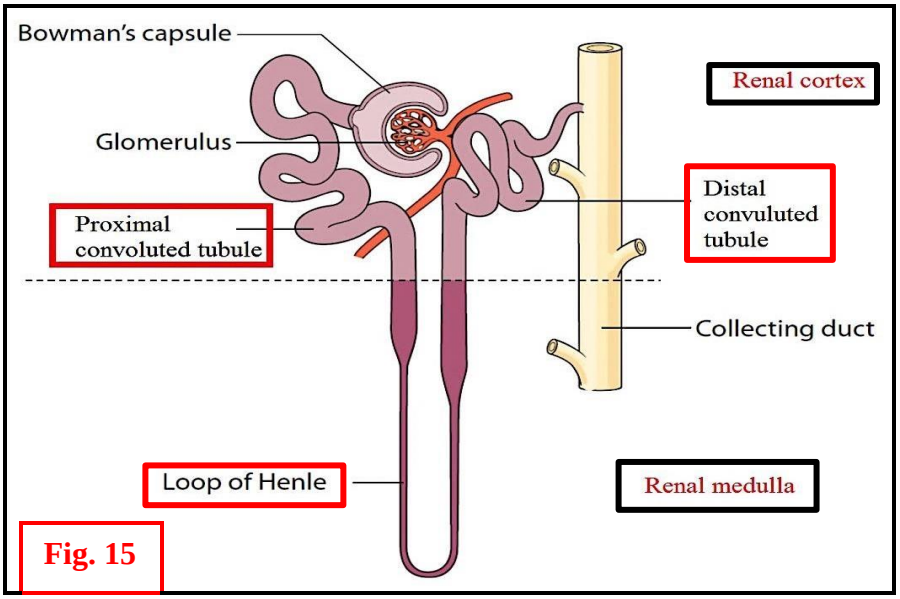


Fig. 15

	Proximal Convoluted Tubules	**Distal Convoluted Tubules**
Site	Labyrinth of cortex	Labyrinth of cortex
Shape	Highly convoluted	Less convoluted
Length	15 mm	5 mm
Diameter	60 µm	30 µm
Lumen	Narrow	Wider
Lining cells	4: 5 cells - Cuboidal epith. - Dark acidophilic cytoplasm - Apical striated border [Microvilli] - Lateral non-clear interlocking cell membranes - Basal striations [Numerous infoldings of the basal membrane and many mitochondria in-between]	6: 8 cells - Low cubical epith. - Paler cytoplasm - Less apical striation [Few microvilli] - Less basal striations[Few mitochondria]
Function	1- Absorption of glucose, amino acids, salt, and water 2- Elimination of organic salts, drugs, and toxins.	1- Regulation of salt and water level(under effect of aldosterone) 2- Active secretion of potassium and hydrogen ion in urine

Loop of Henle

Hairpin-like tubule located in medullary tissue (medullary ray and medulla).

- Formed of two limbs:

1-Descending limb: a-Initial thick segment: Lined by cuboidal cells.
b-Thin segment: Lined by simple squamous cells.

2-Ascending limb: a-Thin segment: Lined by simple squamous cells.
b-Thick segment: Lined by cuboidal cells.

- Function: Formation of hypertonic urine.

Juxtaglomerular (JG) apparatus

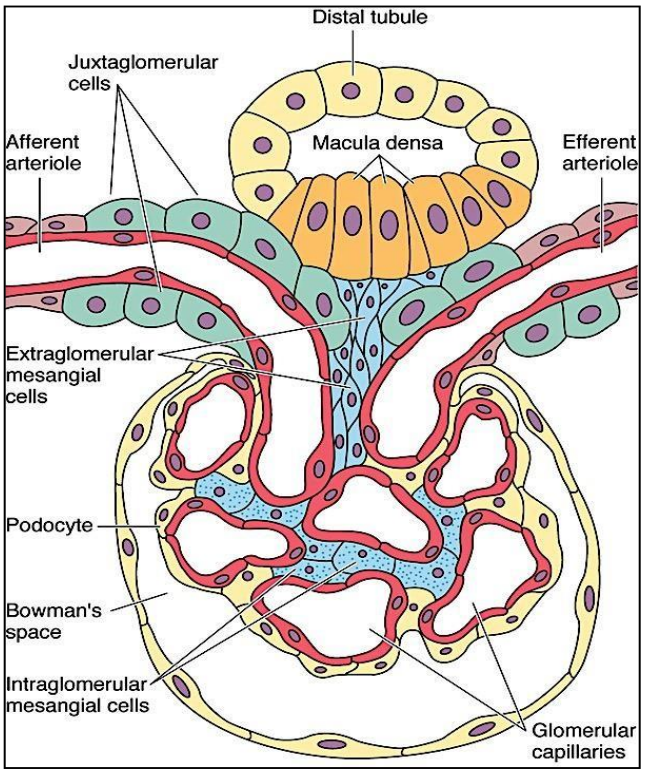


Fig.16

- Site: At the vascular pole of renal corpuscles; helps regulate blood pressure (**Fig.16**).

- Components:

1- Juxta-Glomerular cells:

- Modified smooth muscle cells of tunica media of afferent arteriole.
- Richly innervated by sympathetic nerve fibers.
- Cytoplasm has many acidophilic secretory granules containing renin.

2-Macula densa [Dense spot]:

- Cluster of modified cells in the wall of distal convoluted tubule fitting between afferent &efferent arterioles and adjacent to JG cells.

- Cells become taller and crowded with clustered apical nuclei which gives the appearance of a "dense spot".
- Cells have numerous microvilli and infra-nuclear Golgi apparatus.

N.B: The basement membranes of juxtaglomerular cells and macula densa are lost at this point permitting intimate contact between both structures.

3-Extra-glomerular mesangial cells (Polar cushions):

- Occupy the space between juxta-glomerular cells, macula densa and efferent arteriole.
- Have supportive function.

- Function of Juxta-glomerular apparatus:

- Macula densa acts as osmoreceptors monitoring sodium level and volume of urine in distal tubules.
- In hypovolemia or hypotension → Macula densa stimulate adjacent JG cells to secrete renin (A hormone that regulate blood pressure).

Collecting Tubules and Ducts and Extrarenal Passages

- They are not part of the nephron. They have separate embryological origin.
- Later in the development, they join the nephron to form a continuous structure.

- Components:

1- Collecting tubule: (Fig.17)

- Small collecting tubule drains urine from the distal convoluted tubule of 5: 10 nephrons in the cortical labyrinth.
- Lined by simple cuboidal cells with distinct lateral boundaries.
- Enters the medullary ray in the cortex and descends into the medulla.
- Joins with other collecting tubules to form the large ducts of Bellini (Papillary ducts).
- Function: Aids in concentrating the urine (Under effect of ADH).

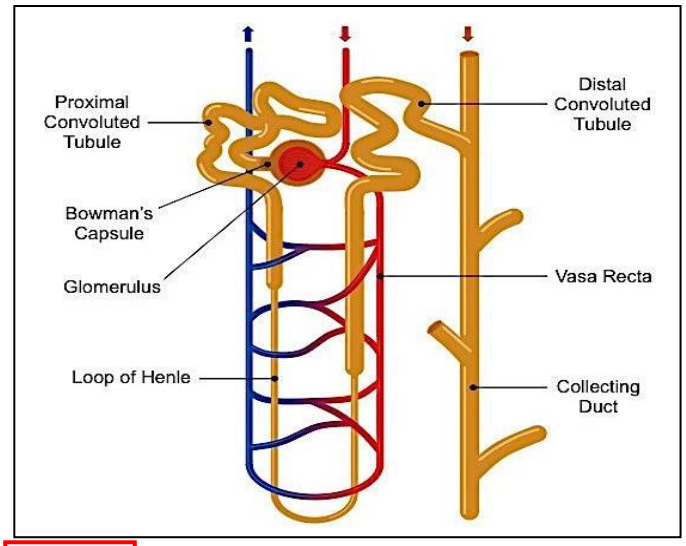


Fig.17

2- Papillary ducts (Ducts of Bellini): (Fig.18)

- Located deep in the medullary pyramids.
- Lined by simple columnar epithelium.
- Empty into the minor calyx at the apex of each pyramid.

3- Renal calyces:

Minor calyx:

- Funnel-shaped structure (one for each pyramid) into which the renal papilla projects.
- Urine flows from the pyramid into a minor calyx.
- Several minor calyces unite to form a major calyx.

Major calyx: Four or five per kidney, formed by the confluence of minor calyces.

Minor and major calyces are lined by transitional epithelium.

4- Renal pelvis:

- Expanded origin of the ureter (Formed by the union of major calyces).
- Lined by transitional epithelium.

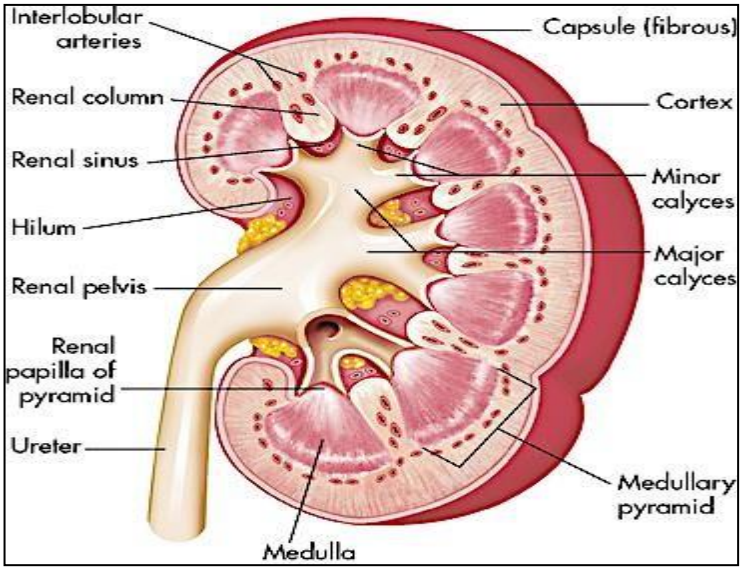
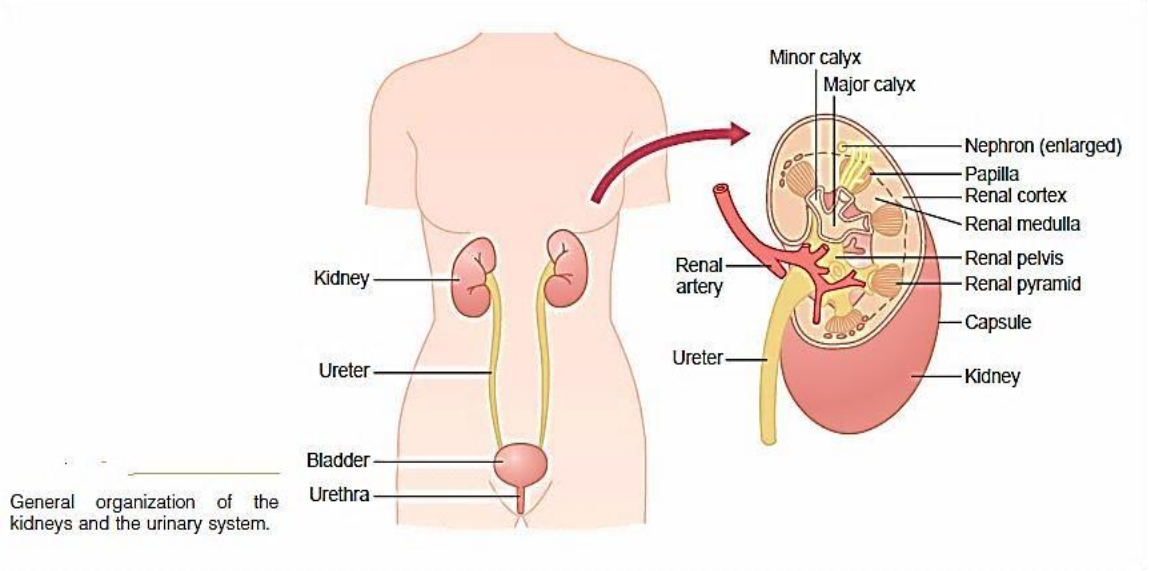


Fig.18

Physiology of the Urinary system

1. The Kidneys:



General organization of the kidneys and the urinary system.

- Importance of the Kidney:

The Kidney are largely responsible for maintenance of constant internal environment through:

1- Excretion of waste products: Urea, creatinine and uric acid.

2- Control of volume, osmotic pressure and electrolyte content of the extracellular fluid.

3- Endocrine functions:

a) Renin – Angiotensin mechanism which regulates ABP.

b) Erythropoieitin hormone which stimulates Erythropoeisis (so, there is anemia in kidney diseases).

c) Formation of 1-25 dihydrocholecalciferol which control Ca^{++} and PO_4 Plasma levels

d) Secretion of prostaglandins (PGE, PGI2) & bradykinin: they are paracrine hormones that regulate renal blood flow.

4- Regulation of arterial blood pressure:

a) short term: through renin angiotensin system.

b) long term: excretion of Na+ & H_2O.

5- Regulation of acid base balance:

a) Elimination of acids e.g., sulphuric & phosphoric acids.

b) Regulation of buffer stores.

6- Gluconeogenesis: during prolonged fasting.

❖ Glomerular Filtration Rate: GFR

***Glomerular Filtrate:** is the fluid that filters through glomeruli into Bowman's capsule, consists of plasma without plasma proteins.

*Glomerular Filtration Rate: is the amount of glomerular filtrate formed each minute in all nephrons of both kidneys.

It equals : 125 ml/min - 180 litre/day (kidney filters in one day a volume of fluid that equals 60 times that of plasma volume).

***Glomerular Capillary Membrane:** **is formed of 3 layers (Fig. 19):**

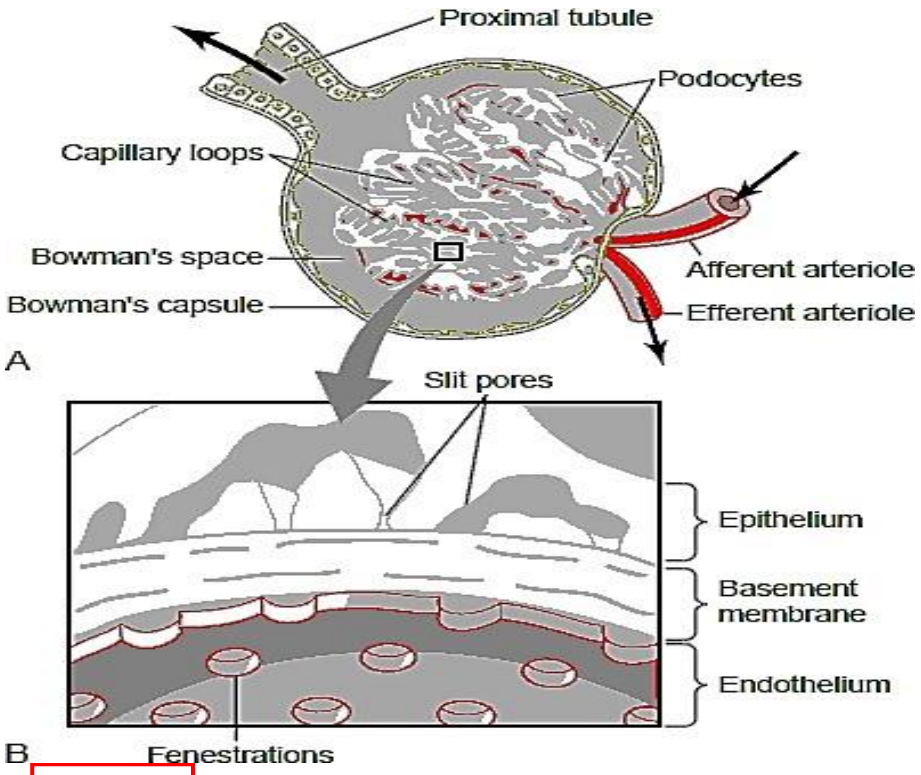


Fig.19

1) **Capillary endothelium**: which have wide pores called fenestra 70-90 nm in diameter (not barrier for plasma protein).
2) **Basement membrane:** which has no pores, it is negatively charged forming anionic sites that repel anions of plasma (e.g., plasma proteins).
3) **Bowman's capsule epithelium:** formed of podocytes with slit pores (25nm).

***Renal Blood Flow** = 1200 ml/min, **plasma flow** = 625 ml/min so, the **filtration Fraction** is the fraction of renal plasma that become filtrate.

It is equal $\frac{125}{625} = 20\%$

***Forces causing glomerular filtration:**

(1) Hydrostatic pressure of glomerular capillary (HP_{GC}) (**60** mmHg)

- It helps filtration.
- It is the highest capillary pressure all over the body because:
  a- The renal artery arises directly from the abdominal aorta at a right angle.
  b- Afferent arterioles are short & straight branches.

c- Diameter of the efferent arteriole is 1/3 that of the afferent, which raises the pressure & increase the resistance.

(2) Colloidal Osmotic Pressure of Bowman's capsule (CO_{BC}) (zero) as no protein in Bowman's capsule (protein is not filtered). It helps filtration.

(3) Colloidal Osmotic Pressure of Glomerular capillary (CO_{GC}) average = **32**mmHg

This force opposes filtration due to the osmotic power of plasma proteins.

(4) Hydrostatic pressure of Bowman's capsule (HP_{BC}) (**18** mmHg):

It opposes filtration.

The Net filtering forces or the filtration pressure (NFF)

NFF = CHP + COPB – (COPG + HPB)

= 60 + 0 – (32 + 18)

= 60 – 50 = 10 mmHg

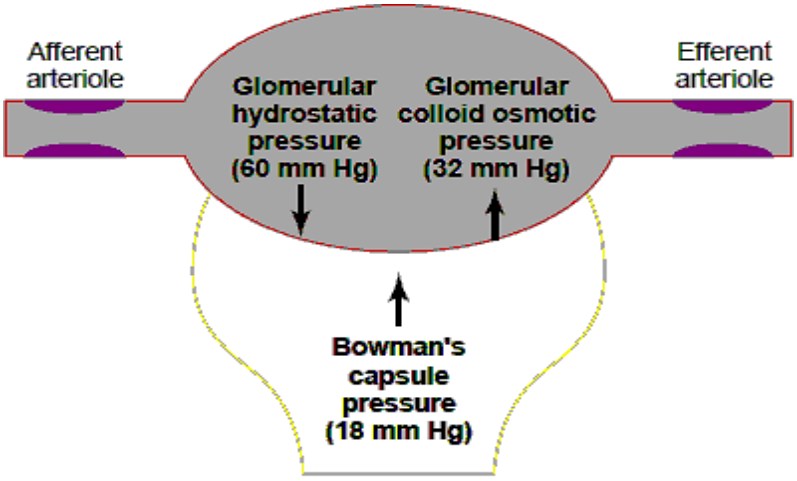


Fig.20

*** Factors affecting GFR**: (**Fig.20**)

(1) Changes in glomerular hydrostatic pressure (GHP):

Glomerular Hydrostatic Pressure is affected by:

A) Afferent arteriolar dilatation (by prostaglandin & bradykinin) leads to increase HP_{GC} → increase GFR.

B) Afferent arteriolar constriction (by sympathetic & adenosine) leads to decrease HP_{GC} → decrease GFR.

C) Moderate Efferent arteriolar constriction leads to increase HP_{GC} → slight increase of GFR.

D) Severe efferent arteriolar constriction → plasma remains for a longer time in glomerulus with more filtration with more increase

in colloidal osmotic pressure (O.P) → decrease GFR. It is called paradoxical decrease in GFR despite elevated HP_{GC}.

(2) Changes in glomerular colloidal osmotic pressure (OP_{GC})

Increase in OP_{GC} (as in dehydration) leads to decrease GFR.

Decrease in OP_{GC} (as in hypoproteinemia) leads to increase GFR.

(3) Increase hydrostatic pressure in Bowman's capsule (HP_{BC}):

As in urinary tract obstruction → decrease GFR.

(4) Increase colloidal osmotic pressure in Bowman's capsule (OP_{BC}):

As in increased glomerular membrane permeability → increase GFR.

(5) Changes in Arterial blood pressure ABP & or renal blood flow :

GFR is kept constant despite of changing ABP between 90 - 200 mmHg. This is called **autoregulation** of GFR. The mechanisms involved in autoregulation of GFR are:

- Myogenic mechanism: increased stretch of afferent arterioles causes smooth muscle contraction
- Flow-dependent mechanism (tubuloglomerular feedback): increased GFR increases flow to distal nephron. The macula densa senses distal flow rate; increased flow causes release of mediator(s) which constricts afferent arteriole.

- Plasma Clearance:

***Definition:** The volume of plasma (in ml) that is cleared from a certain substance which is excreted in urine/min.

***Calculation:**

Amount of substance cleared/min = amount of substance excreted in urine/min

$C \times P = U \times V$

Where: C is volume of cleared plasma/min

P is the concentration of the substance in plasma

U is the concentration of substance in urine

V is the volume of urine/min.

$$C = \frac{U \times V}{P}$$

1) A Substance that is filtered freely and neither reabsorbed nor secreted by the renal tubules will be cleared from plasma only by glomerular filtration. Its clearance equal GFR. For example: inulin.
2) A substance that is reabsorbed by the renal tubules will have clearance below GFR. Since tubular reabsorption returns the filtered substance back to the blood, it decreases its removal (clearance) from the plasma e.g., urea and K^{+}.
3) A substance that is secreted by the renal tubules will have clearance above GFR. Since tubular secretion increases its removal (clearance) from the plasma e.g., creatinine.

**** Importance:**

1- It is an early index of renal disease.
2- It is used for measurement of GFR using inulin or Mannitol.
3- It is used for study of behavior of different substances.

Substance	Clearance	Behavior
Inulin	125 ml/min	Neither reabsorbed nor secreted
Urea, K^+	< 125	Partially reabsorbed
Creatinine (140)	125 – 625	Partially secreted
PAHA	625	Completely secreted
Ammonia	>625	Completely secreted + manufactured by kidney
Glucose	Zero	Completely reabsorbed

4- Determination of effective renal plasma flow ERPF: A substance as Para Amino Hippuric Acid" PAHA" is completely secreted through a single circulation in kidneys. Its clearance = 625 ml/min.
5- Clearance of endogenous substance as that of urea & creatinine: is preferred in investigating renal functions to avoid administration of exogenous substances.

**** Disadvantage:**

It gives the net effect and not the detailed study of renal tubule e.g. K^+ clearance = 75 ml/min which suggests that K^+ is partially reabsorbed but K^+ is 65% reabsorbed in Proximal Convoluted Tubules "PCT" & then secreted in Distal Convoluted Tubules "DCT".

❖ Measurement of GFR:

1. Inulin clearance test:

Large dose of inulin is injected intravenously & followed by sustained infusion to keep arterial plasma level constant.

Inulin is:

a) A polymer of fructose MW = 5200
b) Neither reabsorbed, nor secreted by renal tubule, i.e., amount filtered = amount excreted.
c) Non toxic.
d) Not metabolized.
e) Not stored by kidney and not affect GFR.
f) Can be easily measured in urine & plasma.

Amount filtered = Amount Excreted

$C \times P = U \times V$

C is the volume of glomerular filtrate/min (unknown).
P is the concentration in plasma which is equal to that in filtrate.
U is the concentration in urine.
V is the volume of urine/min.

$$GFR = \frac{U \times V}{P} = 125 \text{ ml/min}$$

2. Creatinine Clearance:

Creatinine is an endogenous substance that is formed from creatine in muscle. It is easily measured.

a) Freely filtered.
b) Not reabsorbed.
c) Partially secreted by the renal tubule.

❖ Specific Functions of Different Tubular Segments

* Functions of Proximal Convoluted tubules:

The tubular epithelium of proximal tubules:

a) Are highly metabolic, having a large number of mitochondria.
b) Have extensive surface area on both luminal (brush border) & basal (extensive channels) borders. Both a & b facilitate proximal tubular function.

[1] Reabsorption of 65 % of filtered Na^+, H_2O, Cl, K**,** Most of HCO3-

Na^+: primary active transport:

– In upper half of proximal tubules: it is coupled by active transport of glucose, amino acids (a.a.).
– In lower half of proximal convoluted tubule: it is accompanied by passive diffusion of Cl

- Cl^-, H_2O: Passive reabsorption secondary to Na^+
- Partial reabsorption of urea: back diffusion secondary to H_2O reasborption.

[2] Secretion of:

H^+: Counter transported with Na^+ at luminal border.
Organic substances: as bile salts, oxalate, urate, catecholamines
Drugs: as penicillin, salicylate & PAH acid.
Uric acid & creatinine
NB: Fanconi Syndrome is due reduction of ATP in proximal convoluted tubules (due to toxins or vit. D deficiency → decrease reasborption of Na^+, glucose, a.a. resulting in metabolic acidosis, glucosuria, amino aciduria.

[3] Synthesis of : Ammonium from glutamine.

* Functions of loop of Henle:

1) Thick ascending limb:

- Reabsorption of 25% of filtered Na, K, cl, (Na-K-2CL) co transport and some Ca & Mg & few HCO_3.
- Secretion of H So, the fluid entering the tubule is hypotonic.

2) Thin descending limb:

- Reabsorption of 20% of filtered water.
- So, fluid reaching the tip is hypertonic.

*** Functions of Distal convoluted tubules (DCT) & cortical collecting tubules (CT):**

(1) First half of DCT (diluting segment):

a) Absorption of Na^+, K^+, Cl^-

b) Impermeable to H_2O, Urea (like thick ascending limb).

c) H+ secretion.

(2) Second half of DCT & cortical CT:

a) absorption of Na^+ in exchange with K^+ secretion under effect of aldosterone (active by Na^+-K^+ ATPase pump at the basal border) These cells are called **principal** cells.

b) Secrete H^+ & reabsorb HCO_3 using H^+ ATPase transport mechanism (independent on Na^+). These cells are called **intercalated** cells (I cells).

c) Impermeable to urea.

(3) Facultative H_2O reabsorption under effect of ADH (**5%**).

(4) Increase reabsorption of Ca^{++} by primary active transport (under parathormone effect).

(5) Ammonium synthesis from glutamine.

***Functions of Medullary collecting duct:**

1) Concentration of urine: together with action of loop of Henle by facultative H_2O reabsorption under effect of ADH.
2) Back diffusion of urea to interstitium maintaining hyperosmolarity of medullary interstitium.
3) Na^+ reabsorption.
4) H^+ secretion by primary active transport.
5) Synthesis of ammonia from glutamine.

   Glutamine $\xrightarrow{\text{glutaminase}}$ NH_3 + glutamic acid

   Glumatic acid $\xrightarrow{\text{glutamic dehydrogenase}}$ NH_3

   NH_3 acts as hydrogen acceptor and then transformed into NH_4 excreted in urine until pH of tubular fluid becomes 6.9 (max. acidifying power of Proximal convoluted tubules).

❖ Renal handling of sodium (Na^+ reabsorption)

Na^+ accounts for over 90% of osmotically active particles in extracellular fluid "ECF" so, determine extracellular fluid volume.

***Mechanism:**

1) At basal border: primary active, against electrochemical gradients. Na^+ is actively pumped, by Na^+-K^+ ATPase from inside tubular cells of P.C.T across basal border to intercellular space.
   - 3 Na^+ are pumped out.
   - 2 K^+ are pumped inside the cell.

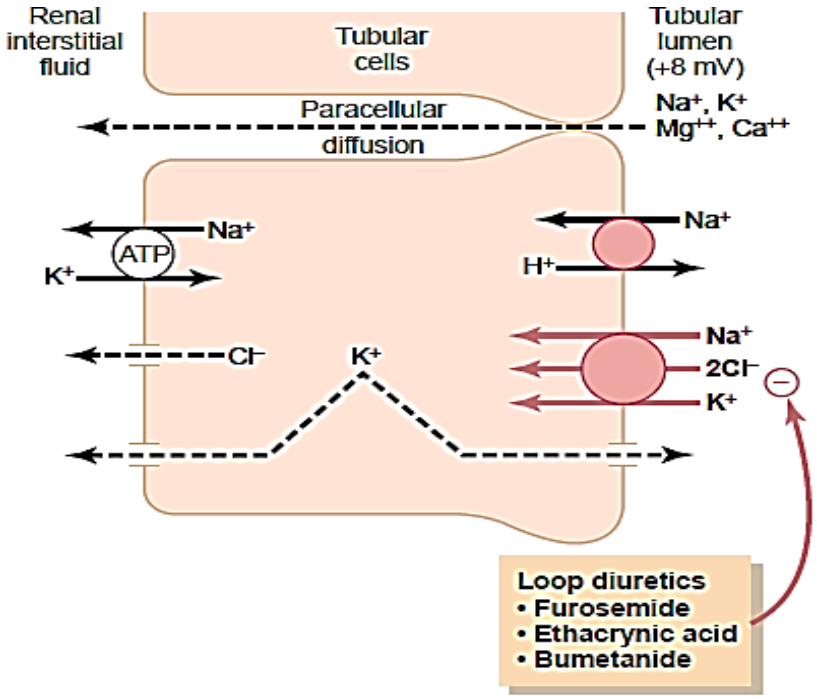
   This creates a negativity inside the cell (-70 mv).
2) At luminal border: passive.

   The pump creates passive diffusion of Na^+ from tubular lumen into tubular cells down an electrochemical gradient.

*** Sites of Na^+ reabsorption** in the nephron :96-99% of Na^+ is reabsorbed.

1) At proximal tubules: Primary active reabsorption of Na^+
   - In upper half: coupled by co-transport of glucose & a.a & organic acids (lactate & citrate) & HCO_3, and H^+ secretion by Counter transport.
   - In lower half: Na^+ is reabsorbed, accompanied with:
     - Cl-, HCO_3 reabsorption, passive by electrical gradient.
     - H_2O reabsorption, passive by osmotic gradient.

2) At loop of Henle: Only in ascending limb, 30% of filtered Na^+ is reabsorbed (No Na^+ channels in descending limb).



Mechanisms of sodium, chloride, and potassium transport in the thick ascending loop of Henle. The sodium-potassium ATPase pump in the basolateral cell membrane maintains a low intracellular sodium concentration and a negative electrical potential in the cell. The 1-sodium, 2-chloride, 1-potassium co-transporter in the luminal membrane transports these three ions from the tubular lumen into the cells, using the potential energy released by diffusion of sodium down an electrochemical gradient into the cells. Sodium is also transported into the tubular cell by sodium-hydrogen counter-transport. The positive charge (+8 mV) of the tubular lumen relative to the interstitial fluid forces cations such as Mg^{++} and Ca^{++} to diffuse from the lumen to the interstitial fluid via the paracellular pathway.

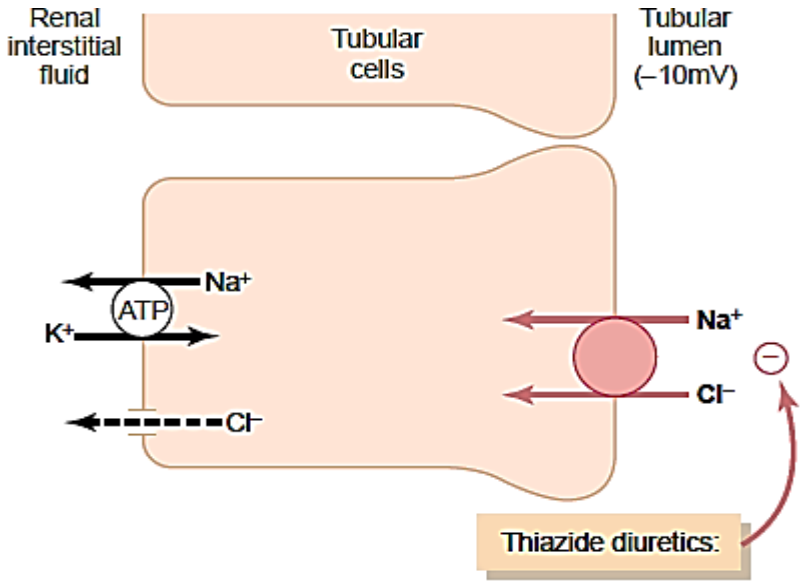
Fig.21

→ In the thin part, Na^+ reabsorption is limited (Passive).

→ In the thick part, Na^+ reabsorption (25%) is active; Cl^- is secondary to it (1 Na^+, 2Cl^-, 1K^+ (co-transport)).

3) At distal convoluted tubules + collecting tubules: 3%
   - Under the control of aldosterone, variable amounts of Na^+ are reabsorbed and associated with → Cl^-, HCO_3 reabsorption passively.

→ K^+, H^+ secretion (counter transport).



Mechanism of sodium chloride transport in the early distal tubule. Sodium and chloride are transported from the tubular lumen into the cell by a co-transporter that is inhibited by thiazide diuretics. Sodium is pumped out of the cell by sodium-potassium ATPase and chloride diffuses into the interstitial fluid via chloride channels.

Fig.22

**** Regulation of Na+ excretion:**

(1) Rate of tubular flow & GFR:

Slow rate of flow → increase tubular reabsorption of Na^+.

As in decrease GFR which initiates tubuloglomerular feedback mechanism (as discussed before).

Increase GFR →increase Na^+ filtered → increase Na^+ reabsorbed → slight increase in Na^+ excretion i.e., proximal tubules reabsorb constant % of filtered load of Na^+ & H_2O.

(2) Pressure Naturesis (Effect of increased Arterial Blood Pressure "ABP" on Na^+ excretion):

Increase ABP → increase Na^+, H_2O excretion to regulate ABP & return it to normal. It is compensatory mechanism independent of nerves or hormones.

(3) Concentration gradient:

Na^+ reabsorption has no transport maximum (Tm) in proximal convoluted tubules. So, reabsorption is determined by 2 factors:

- Concentration gradient → increase Na^+ in proximal tubules → increase reabsorption of Na^+
- The time that the fluid remains in the tubule: The more the time, the more the reabsorption.

However, in the distal tubule, Na^+ transport exhibits a transport maximum "Tm".

(4) **Sympathetic stimulation:** increase Na+ reabsorption
- direct on PCT & thick ascending loop of Henle
- increase renin & angiotensin II

(5) **Hormones:**

-**Aldosterone**: Acts on distal tubules & cortical collecting tubules.
- Increases Na^+ reabsorption, Cl^- reabsorption.
- Increases K^+ & H^+ secretion.
- Mechanism: induces synthesis of protein that increase number of open channels in luminal border & increase Na^+-K^+ATPase at base.

-**Angiotensin II:** leads to Na^+ retention
++ aldosterone
Direct effect on PCT (++ Na-K pump & H^+ pump)
Constrict efferent arteriole (-- hydrostatic press & ++ osmotic Pressure of peritubular capillaries)

-**Glucocorticoids:** ↑ Na^+ reabsorption through their weak mineralocorticoid effect.

-**Sex hormones** especially Estrogen: ↑ Na^+ reabsorption as they have mineralocorticoid effect (before menses).

-**Atrial Natriuretic peptide** "ANP": Na^+ excretion
- increase GFR by relaxation of mesangial cells & VD of Afferent arteriole & VC of efferent arteriole.
- inhibits renin secretion.
- direct on collecting duct (inhibits Na-K^+ pump & Na^+ channels).

(6) **Effect of diuretics:**

Diuretics are substances which increase urine volume

a- Osmotic diuretics: which decreases Na^+ & H_2O reabsorption at proximal convoluted tubules.
E.g., Mannitol & glucose which are not absorbed → they will retain water & increase volume of urine & increase excretion of Na^+ in urine → they are primary diuretics & secondary naturetic

b- Diuretic drugs (loop diuretics): which decreases Na^+ reabsorption at thick part of loop of Henle e.g., lasix (Furosemide) → the excreted Na^+ retains H_2O with it → They are primary naturetic & secondary diuretics

c- Diuretics that inhibit aldosterone as Spironolactone or aldactone. It decreases Na^+ reabsorption from DCT & CD → Na^+ loss & K^+ retaining (it acts on Na^+-K^+ exchange mechanism).

❖ Renal handling of glucose (Glucose reabsorption)

Glucose is: 1- Completely reabsorbed.
2- In proximal convoluted tubule (upper half)
3-By an active process (secondary active)

Glucose to be reabsorbed via tubular cells, it has to cross its luminal and basal borders.

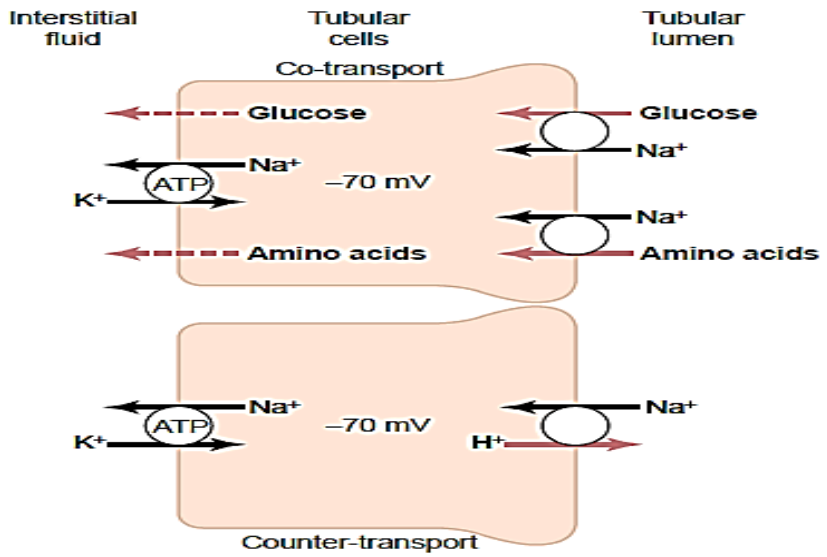
(1) **At luminal border**:

- By secondary active mechanism (no energy is used directly from ATP)
- It enters the cell against concentration gradient.

- A carrier (termed SGLT-2 = sodium dependant glucose transporter) binds both Na^+ & glucose at the luminal brush border where Na^+ diffuses along electrochemical gradient & glucose actively against concentration gradient.

(2) At basal border:

- By facilitated diffusion, passive, the glucose passes to the extra cellular fluid & blood.
- The carrier needed here is not Na^+ dependent. It is termed (GLT-2) glucose transporter.



Mechanisms of secondary active transport. The upper cell shows the *co-transport* of glucose and amino acids along with sodium ions through the apical side of the tubular epithelial cells, followed by facilitated diffusion through the basolateral membranes. The lower cell shows the *counter-transport* of hydrogen ions from the interior of the cell across the apical membrane and into the tubular lumen; movement of sodium ions into the cell, down an electrochemical gradient established by the sodium-potassium pump on the basolateral membrane, provides the energy for transport of the hydrogen ions from inside the cell into the tubular lumen.

Fig.23

**** Study of glucose reabsorption: -**

- **Tubular load "TL" of glucose**, is the total amount of glucose that is filtered in glomerular filtrate/min = (**125** mg/min)

"TL" = GFR × concentration of glucose/ml plasma

125 ml/min × 1 mg glucose/ml plasma [100 mg/100 ml]

- **Glucose Renal Threshold**:
- This is the maximal concentration of glucose in plasma above which glucose appears in urine.
- **Normal glucose plasma level = 70-110 mg%**; Up to 180 mg%, all glucose filtered is reabsorbed. The glucose appears in urine at a plasma concentration above **180 mg%** in venous blood & **200 mg %** in arterial blood.

Tubular Maximum of Glucose "TMG":

Is the maximal amount of glucose which can be reabsorbed/min = **300** mg/min in female & **375** mg/min in male.

Above the renal threshold, glucose excretion rises. Finally, glucose reabsorption reaches a maximum rate called Transport Maximum for glucose (TMG) when the carrier for glucose is completely saturated. TMG depends on reabsorbed power of different nephrons which depends on amount of carrier protein.

** **Glucosuria:** is appearance of detectable amount of glucose in urine.

Causes:

1- **Diabetes Mellitus:** decrease insulin → increase blood glucose above 180 mg% → increase tubular load of glucose above TMG.
2- **Stress Hormones:** they lead to hyperglycemic glucosuria.
3- **Renal Glucosuria:** This is a hereditary disease in which the number of glucose carrier decreases or the affinity of the carrier towards glucose is reduced. This lower renal threshold &TM to about 100 mg%. Thus, glucosuria occurs at normal fasting glucose level.
4- Other **monosacchrides** as galactose, xylose & fructose, when present simultaneously with glucose they depress its transport. This is called "competition for transport".
5- **Oubain** which block Na^+ -K^+ ATPase.
6- **Phlorizin** which blocks sugar access to the carrier protein.

❖ Mechanism of Water Reabsorption and Urine Concentration:

About 180 liter/day of fluid filtered by both kidneys & Urine volume is about 1 liter/day.
I.e.,179 liter of H_2O is reabsorbed / day (99%).
H_2O reabsorption in kidney is 2 types:

	Obligatory	Facultative
Amount:	87%	13%
Mechanism	secondary to solutes reabsorbed e.g.Na^+	Na^+ independent
Effect on urine	Not affect urine concentration	Can affect urine concentration
ADH	Not affect it	It depends on it

** **Reabsorption of H_2O in different tubular segments: (Figs. 24,25)**

(1) Proximal convoluted tubules:

- 65 % is obligatory reabsorbed secondary to active transport of solutes as Nacl, glucose, amino acids.
- It occurs through H_2O channels called aquaporin-1(protein in nature) located at luminal border of tubular cells of PCT.

(2) Loop of Henle:

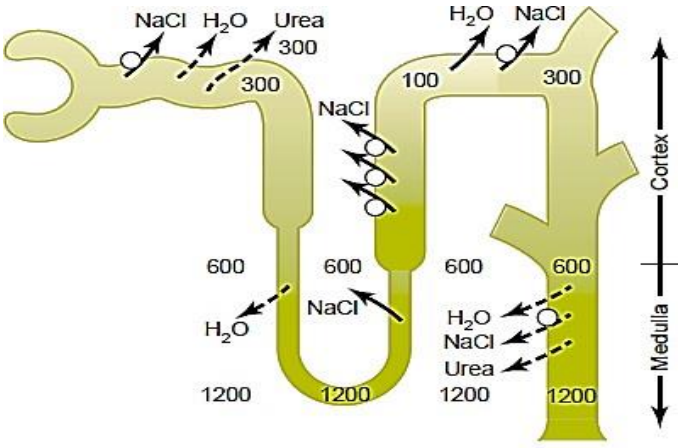
- 15% of H_2O is reabsorbed by descending limb.

(3) Distal convoluted tubule:

- 7% of H_2O is reabsorbed.

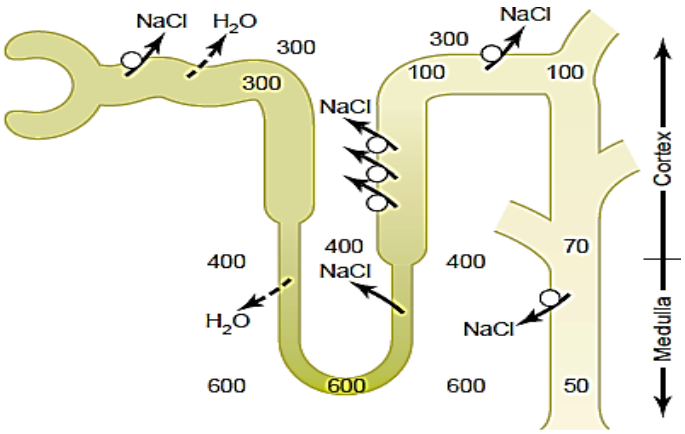
(4) Late distal tubule & collecting duct (cortical & medullary):

- Under effect of antidiuretic hormone (ADH): variable 13%.



Formation of a concentrated urine when antidiuretic hormone (ADH) levels are high. Note that the fluid leaving the loop of Henle is dilute but becomes concentrated as water is absorbed from the distal tubules and collecting tubules. With high ADH levels, the osmolarity of the urine is about the same as the osmolarity of the renal medullary interstitial fluid in the papilla, which is about 1200 mOsm/L. (Numerical values are in milliosmoles per liter.)

Fig.24



Formation of a dilute urine when antidiuretic hormone (ADH) levels are very low. Note that in the ascending loop of Henle, the tubular fluid becomes very dilute. In the distal tubules and collecting tubules, the tubular fluid is further diluted by the reabsorption of sodium chloride and the failure to reabsorb water when ADH levels are very low. The failure to reabsorb water and continued reabsorption of solutes lead to a large volume of dilute urine. (Numerical values are in milliosmoles per liter.)

Fig.25

- It acts on H_2O channels called aquaporin-2 located in the principal cells at luminal border.
- N.B: Aquaporin-3 is located at basolateral membrane of collecting duct for transport of urea, glycerol & water.

**Mechanism of water reabsorption: in collecting tubules depends on:

1- Counter current mechanism: done by loop of Henle → this creates high osmotic pressure in interstitium of renal medulla which pulls water from collecting tubules.

2- Antidiuretic hormone (ADH).

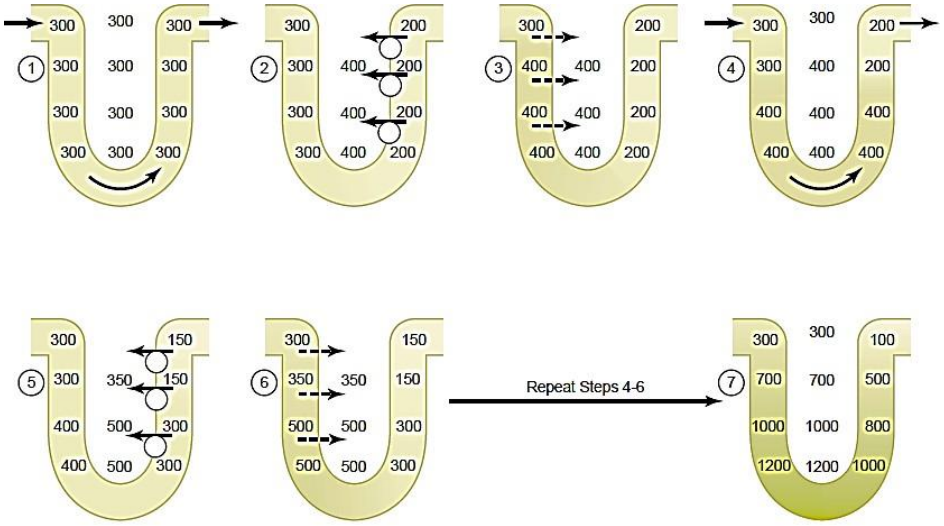
**Mechanism of Urine concentration: (Fig.26)

"Counter Current Mechanism"

This involves 2 main mechanisms:

1) Counter Current multiplier mechanism of loop of Henle.
2) Counter Current exchanger mechanism of Vasa Recta.

[1] Counter Current Multiplier = function of loop of Henle.



Countercurrent multiplier system in the loop of Henle for producing a hyperosmotic renal medulla. (Numerical values are in milliosmoles per liter.)

Fig. 26

(1) The thick part of the ascending limb:

- It is lined by cuboidal epithelium rich in mitochondria.
- Na^+ is actively pumped from the lumen to the interstitium.
- Cl^- is passively reabsorbed secondary to Na^+ (cotransport with sodium).
- (1Na - 2Cl - 1K).
- The wall is impermeable to water being lined by cuboidal epithelium.
- The result is increased osmotic pressure of the interstitial fluid while the tubular fluid delivered to distal convoluted tubules becomes hypo-osmotic.

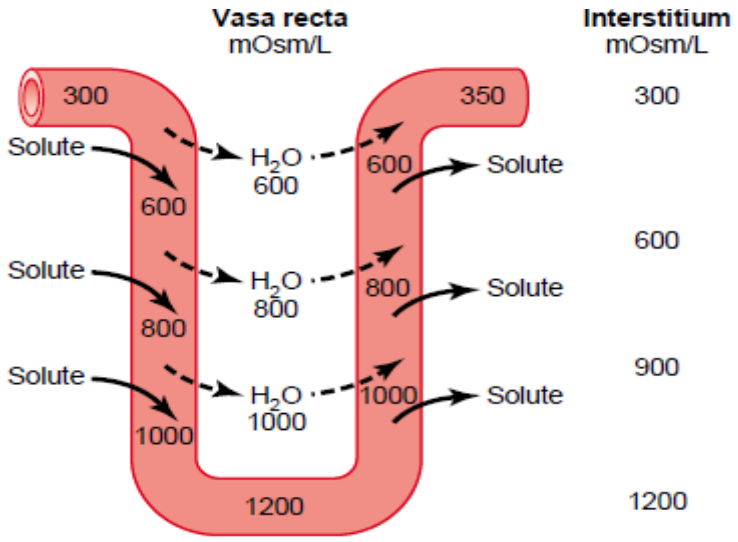
(2) The thin part of the ascending limb:

- It is permeable to Na^+ and Cl^-, so Nacl diffuses passively from the lumen to the interstitium.
- It is impermeable to water.
- The net result of the previous two steps is the creation of the high osmotic pressure in the interstitium of the renal medulla due to passive reabsorbtion of Nacl from the thin part and active reabsorbtion of Nacl from the thick part of the ascending limb.

(3) The descending limb:

- It is lined by simple squamous epithelium.
- It is relatively impermeable to Nacl and urea.
- It is freely permeable to water which diffuses from the lumen to the interstitium under the effect of hypertonic interstitium.
- The result is that the fluid passing down the descending limb becomes more and more hypertonic until it reaches the maximum concentration at the tip of the loop (1200 m.osmole).

Vasa Recta as Counter-Current Exchanger:



Countercurrent exchange in the vasa recta. Plasma flowing down the descending limb of the vasa recta becomes more hyperosmotic because of diffusion of water out of the blood and diffusion of solutes from the renal interstitial fluid into the blood. In the ascending limb of the vasa recta, solutes diffuse back into the interstitial fluid and water diffuses back into the vasa recta. Large amounts of solutes would be lost from the renal medulla without the U shape of the vasa recta capillaries. (Numerical values are in milliosmoles per liter.)

Fig.27

(A) Descending limb of Vasa Recta:

1- Nacl and urea diffuses from the interstitial fluid to the blood along concentration gradient.

2- H_2O diffuses from blood to the interstitium as:

(a) The interstitial fluid is hyperosmotic.

(b) The capillary blood pressure (35 mmHg) is higher than the osmotic pressure of plasma proteins (25 mmHg).

Net result: blood now is hypertonic at the tip of vasa recta.

(B) Ascending limb of Vasa Recta :

1- Nacl and urea diffuse from the blood to the interstitium as the blood now is more concentrated than the interstitium.

2- However, water coming from collecting tubules, descending limb of vasa recta and loop of Henle diffuse from the interstitium to the blood of the general circulation as → a) blood becomes more concentrated than interstitium b) Plasma protein becomes more concentrated → higher osmotic pressure than capillary pressure.

3- The net result: Solutes (Nacl and urea tend to recirculate in the medullary interstitium → (Nacl and urea cycle) while water tends to leave the interstitium and passes to the general circulation. This maintains the hyperosmolarity of the medullary interstitium.

**** Thus, the Vasa recta perform two important functions:**

1- Trapping solutes (Nacl and urea) in the renal medulla.

2- Removing the absorbed water from the medulla to the general circulation.

The role of urea in concentration of urine:

Absorption of urea in the medullary collecting duct (which is highly permeable to urea in the presence of ADH), adds much to the osmolarity of lower medulla, which in turn increases the rate of H2O reabsorption by descending limb of loop of Henle so increasing NacL concentration in the tubular fluid that reach ascending limb.

Urea diffuses from medullary interstitium to the thin ascending limb and to the descending limb of L.H till reaches inner medullary collecting duct to be reabsorbed again by ADH which is known as **urea trapping** or **urea cycling**.

❖ Renal regulation of plasma PH (Acid base balance):

-It takes hours or days (slow) to correct PH.

-In general, the kidneys can excrete variable amounts of H^+ in urine. According to blood PH, acidic or alkaline urine is excreted.

-In acidosis: increased H^+ excretion & urine is acidic. Minimum **pH = 4.5**.

-In alkalosis: less H^+ excreted & urine is alkaline. Maximum **pH= 8**.

-Normally, the pH of urine is **6** (acidic).

The principal mechanisms are:

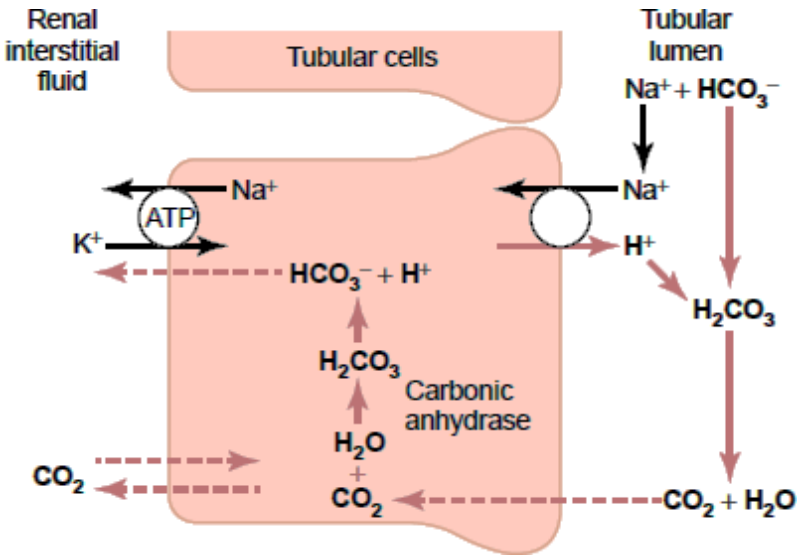
(A) H^+ secretion against bicarbonate Reabsorption.
(B) Production of titeratable acid & bicarbonate regeneration.
(C) Excretion of Ammonia.

(A) H^+ secretion:

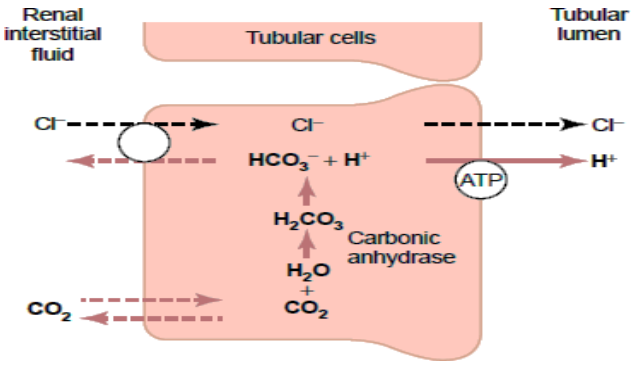
1- Secondary active secretion in proximal convoluted tubules (85%) & thick ascending loop of Henle (10%).
2- Primary active secretion in late tubules (distal tubules & cortical collecting tubules) (5%).

1- Secondary active secretion:

- In tubular cells, CO_2 reacts with water (in presence of carbonic anhydrase) to form carbonic acid.
- Carbonic acid dissociates to H^+ & HCO_3.
- HCO_3 is passively reabsorbed to blood (85 % in proximal convoluted tubules & 10 % in ascending loop of Henle).
- H^+ is actively secreted in exchange with Na^+ (Na^+-H^+ counter transport).
- It uses energy provided by gradient for Na^+ movement across luminal border.
- In lumen of tubules: H^+ reacts with filtered bicarbonate to form carbonic acid which dissociates to CO_2 & H_2O. CO_2 diffuses into the cell.



2-Primary active secretion:



- In tubular cells, CO_2 reacts with water (in presence of carbonic anhydrase) to form carbonic acid.
- Carbonic acid dissociates to H^+ & HCO_3.
- HCO_3 is passively reabsorbed to blood.
- H^+ is actively secreted by specific transport protein (H^+-ATP ase).
- In the lumen of the tubules: H^+ is buffered by phosphate buffer & NH_3.
- It is stimulated by aldosterone.

Factors affecting acid secretion:

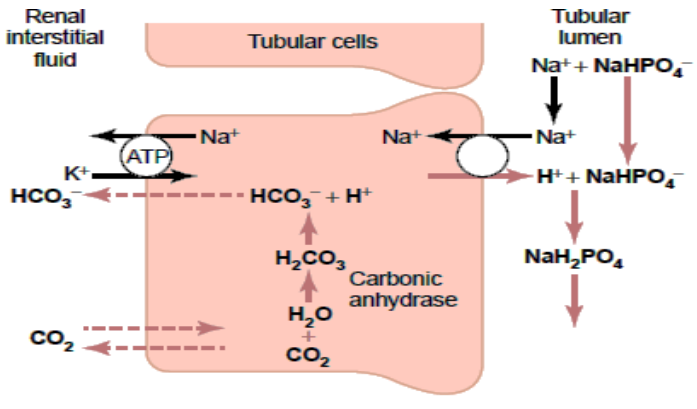
1- aldosterone: stimulates H^+ & K^+ secretion.

2- intracellular CO_2.

3- K^+ concentration intracellular: low K^+→increase H^+ secretion.

(B) Production of titeratable acids & bicarbonate regeneration:

- It occurs in distal tubules & collecting ducts.
- The tubular cells continue to secret H^+ as explained above.
- In the tubular lumen: H^+ reacts with filtered sodium monohydrogen phosphate (Na_2HPO_4) to form sodium dihydrogen phosphate (NaH_2PO_4) which is termed titeratable acid.
- Thus, for each molecule of titeratable acid formed in urine, one HCO_3 is generated and added to blood.
- 20 meq/day titeratable acid are excreted in urine.

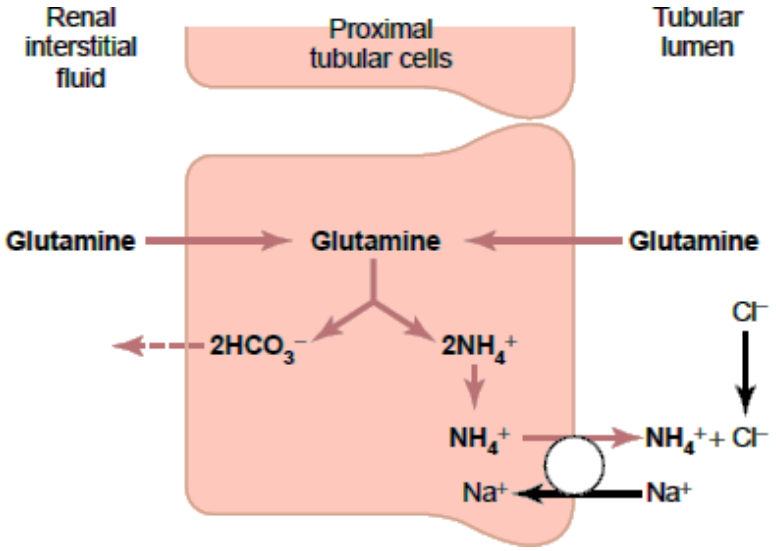


Buffering of secreted hydrogen ions by filtered phosphate ($NaHPO_4^-$). Note that a new bicarbonate ion is returned to the blood for each $NaHPO_4^-$ that reacts with a secreted hydrogen ion.

[C] Excretion of Ammonium in proximal convoluted tubules, loop of Henle & distal convoluted tubules and excretion of ammonia in collecting duct:

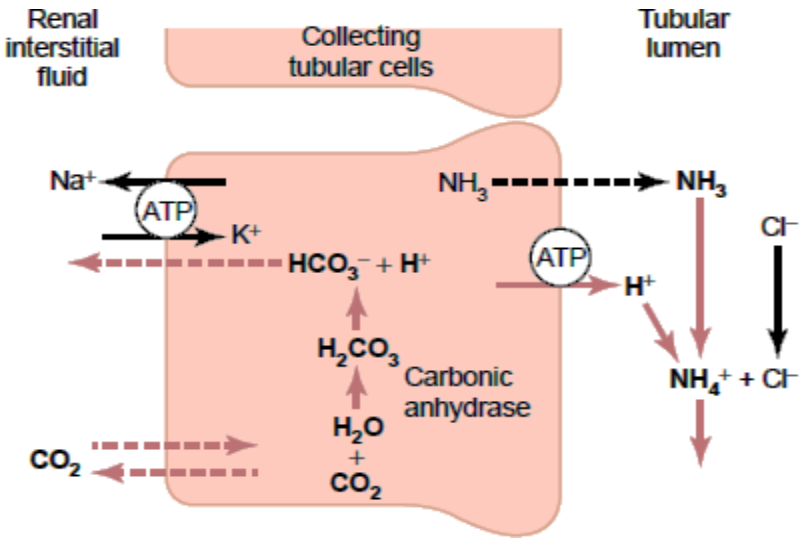
1- Excretion of ammonium (NH_4) in PCT, loop of Henle & DCT:

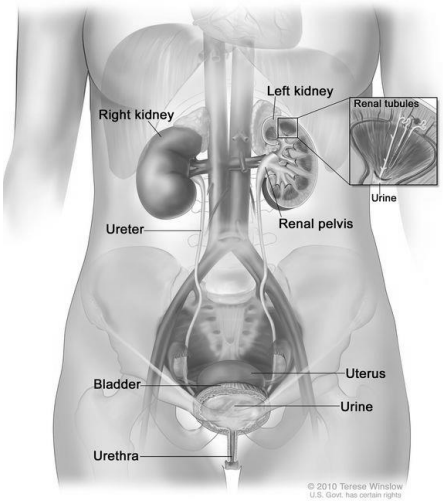
- Ammonium is synthesized in these tubules form glutamine.
- 2 NH_4 + 2 HCO_3 are formed from each glutamine molecule.
- NH_4 is transported into tubular fluid by counter transport in exchange with Na_+.



2- Excretion of ammonia (NH_3) in collecting duct:

- NH_3 is produced by tubular cells from glutamine, glutamic acid, glycine & alanine.
- NH_3 diffuses rapidly to the lumen (fat soluble).
- In the lumen, it acts as a H^+ acceptor and combines with extra H^+ forming NH_4 (ammonium ions). This mechanism is called **diffusing trapping**.
- NH_4 combines with cl^- to form NH_4cl which is slightly acidic allowing excretion of huge amount of H+ without much change in pH of urine (So, NH_4 is the best mechanism in treatment of chronic acidosis).
- For each H^+ excreted, one $NaHCO_3$ is added to blood.





Ureter

URETER

Parts and relations: (10 inches).

1) **Pelvis of ureters:**

- Dilated part of the ureter inside the kidney sinus and surrounded by renal fat.
- It lies in the hilum post to renal vessels.
- It collects urine from major calyces.
- It becomes ureter proper at the pelviureteric junction (lower border of L2).

2) **Ureter proper (abdominal part):** (5 inches).

	Rt	Lt
Post	• L2-5 transverse processes • Psoas major (+ psoas minor, genitofemoral N)	
Ant	• Rt gonadal Vs • Rt colic vessels • Ileocolic vessels • Root of mesentery (containing sup mesenteric vessels)	• Lt gonadal Vs • Sup Lt colic vessels • Sigmoidal vessels • Sigmoid colon & mesocolon

3) **Ureter proper (pelvic part):** (5 inches).

- It crosses ant to common iliac vessels to enter the pelvis.
- Curves to the ischial spine.
- Passes over the levator ani.
- Crossed anteriorly by vas deference in males and uterine A in females.

4) **Intramural part:** (1 inch) passes obliquely in the wall of bladder (superolateral angle of trigone) to form a valve like termination preventing urine reflux.

Physiological constrictions:

1) **Pelviureteric junction:** opposite L2 transverse process.
2) **At the end of common iliac A:** opposite sacroiliac joint.
3) **The intramural part:** opposite iliac spine.

Blood supply: from nearby vessels (renal, gonadal, aorta and IVC, common iliac & int iliac).

Nerve supply:

Autonomic: from T10-11(pain at loin) and T12-L1 (pain at groin). It Communicate with testicular plexus (pain in scrotum).

N.B.: in ureteric colic, direct irritation to genitofemoral N leads to contraction of cremasteric muscle and elevation of testis.

- Histology of Ureter:

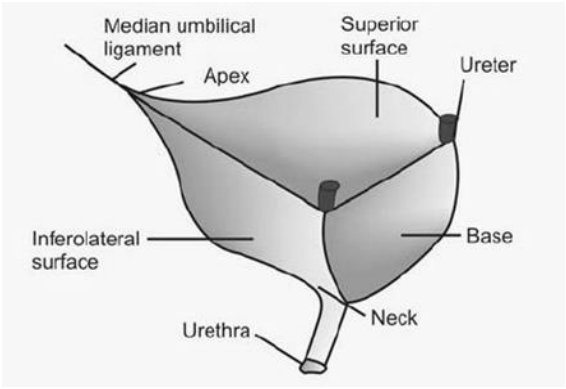
-Muscular tube connecting the renal pelvis and the urinary bladder.

-Formed of mucosa, musculosa & adventitia.

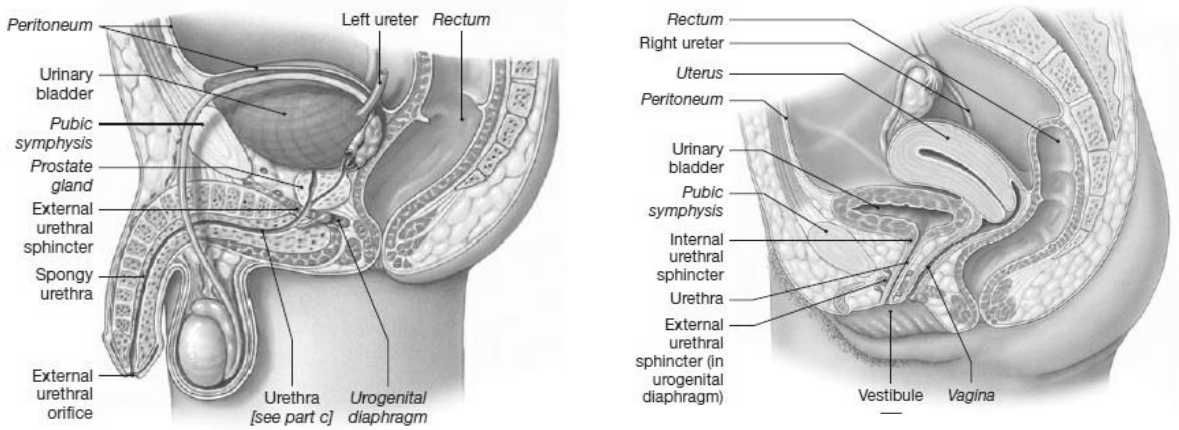
-Lined by transitional epithelium.

-Upper two-thirds has two smooth muscle layers (inner longitudinal and outer circular).

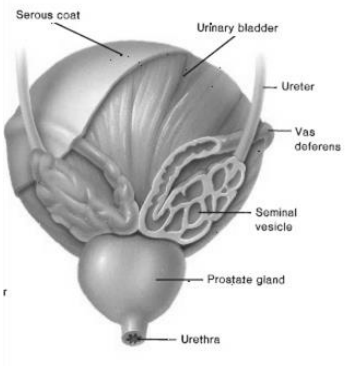
-Lower third has additional third outer longitudinal layer.



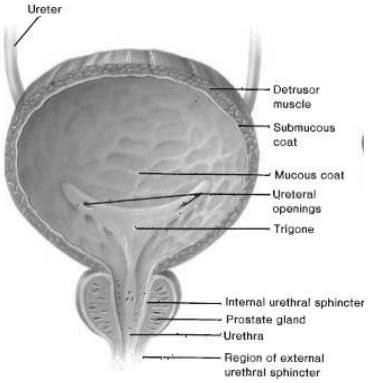
Parts of urinary bladder



Relations of urinary bladder



Posterior relation of urinary bladder in males



Interior of urinary bladder

URINARY BLADDER

Position: in newborn it is abdominal organ. It becomes pelvic at 5 years of age.

Parts and relations:

Superior surface:

In males: small intestines and sigmoid colon.

In females: uterovesical pouch containing small intestines and sigmoid colon separating it from uterus.

Posterior surface (base): between the 2 ureteric openings and the neck

In males: 2 vas differences & their ampullae, 2 seminal vesicles, 2 ejaculatory ducts, prostate and rectum (separated by rectovesical pouch).

In females: vagina (ant wall).

2 inferolateral surfaces:

Ant: symphysis pubis (separated by retropubic space containing fat & vesical venous plexus).

On the sides: levator ani & obturator internus (separated by obturator N & Vs)

Apex (sup angle): meeting of sup & 2 inferolateral surfaces. Lies above symphysis pubis. The median umbilical ligament (obliterated urachus) extends from it to umbilicus.

Neck (inf angle): 1 inch behind and below symphysis pubis. It is fixed by puboprostatic ligament (in males) and pubovesical ligament (in females).

Interior of the bladder:

Mucous membrane: except the trigone, it is loosely attached to the muscle layer (due to different embryological origins). It shows rugae if the bladder is empty and becomes smooth when it is filled.

Ureteric orifices: 2 crescentic slits at the superolateral angles of the bladder

Interureteric ridge: between the 2 ureteric orifices, 1 inch in empty bladder

Trigone: triangular area lining the base. Its mucosa is adherent to the underlying muscle (due to same embryological origin). So, it is always smooth, very rich in blood and nerve supply. It is the most sensitive area for stretching.

Uvula vesica: mucosal elevation of the lower part of the trigone due to enlargement of the median lobe of prostate in old males.

Ligaments of the bladder:

Median umbilical ligament (obliterated urachus): from apex of the bladder to umbilicus.

2 med umbilical ligaments (obliterated umbilical As): from sup surface of bladder to umbilicus.

Lat ligament of the bladder: from sides of the base of bladder to the side of pelvis.

Post ligament of the bladder: from the base of bladder to internal iliac Vs

Puboprostatic or pubovesical ligaments (in males and females respectively): med and 2 lat ligaments, from neck of bladder (and prostate in males) to the back of pubis.

False ligaments: peritoneal folds from bladder to pelvic walls

Blood supply:

Arterial:

Sup vesical As: 2-3 branches of umbilical A supplying sup surface.

inf vesical or vaginal As: (in males and females respectively): 2-3 branches of internal iliac A (anterior division). It supply the base

Venous: vesical venous plexus (on the inferolateral surface) drains into internal iliac V. It communicates with prostatic or vaginal venous plexus

Nerve supply:

Parasympathetic: S2-4 **Sympathetic:** T11-L2

- Histology of Urinary bladder:

- Lined by transitional epithelium specialized to provide for distension of the organ.
- Has thick muscular wall contains three interlacing layers of smooth muscle and a mixture of collagen and elastic fibers.

- Micturition:

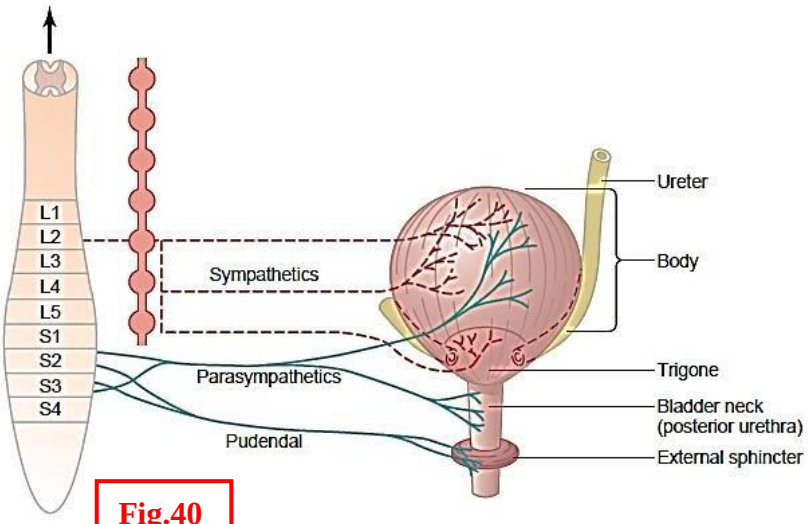
- Emptying the bladder is referred to as micturition, urination, or voiding. It involves the synchronous contraction of the bladder wall muscle (detrusor) and relaxation of the urethral sphincters. These processes are coordinated by a combination of autonomic spinal cord reflexes and voluntary control of the external urethral sphincter which is made of striated muscle. Consequently, micturition, like breathing, is a mixture of reflex and voluntary actions.
- The urinary bladder is progressively filled by inflow of urine from the ureters. At low volumes **(<200–300mL**) the bladder is a relatively compliant organ and filling is accompanied by only modest increases in tension in the bladder wall. At volumes **>300mL**, tension increases more markedly, and this is detected by stretch receptors in the bladder wall smooth muscle. It is at this level of filling that a sensation of fullness is felt in the bladder.
- Impulses from the stretched detrusor muscle are sent, via sensory nerves (**S2–S4**), to the pontine micturition center in the brainstem where the micturition reflex is integrated. In response to these sensory inputs, parasympathetic efferent signals (**S2–S4**) initiate contraction of detrusor which, since it is a syncytium of smooth muscle cells, contracts. This results in increased pressure and tendency towards expulsion of urine and opening of the bladder neck (internal sphincter).
- Voluntary control of the bladder arises largely as a result of the external urethral sphincter. This structure is formed where the urethra passes through the urogenital diaphragm (located in the pelvic arch) which comprises skeletal muscles of the pelvic floor under voluntary, cortical control. Contraction of this sphincter prevents the flow of urine and voluntary relaxation has the reverse effect and initiates the flow of urine during micturition
- Further, voluntary control of micturition arises from inhibitory inputs from cortical and suprapontine centers to the pontine micturition center, which inhibit the micturition reflex until it is socially acceptable to urinate, or the sensation of bladder fullness becomes too intense. Sympathetic nerves from the hypogastric plexus also inhibit contraction of detrusor and aid the inhibition of micturition by higher cortical centers.
- During bladder emptying, sensory receptors in the urethra sense the flow of urine and feedback to the micturition center. This has the effect of enhancing the micturition

reflex and increasing the flow of urine. Contraction of abdominal and pelvic muscles can also increase the pressure on the bladder wall, thus aiding micturition.

- The bladder can be voluntary emptied at any time, even when not full, indicating that higher areas of the brain can initiate the micturition reflex in the absence of afferent input from stretch receptors.
- Voluntary control of micturition can be lost following damage to inhibitory descending pathways in the spinal cord. Such an insult results in urinary incontinence. Furthermore, lesion of the parasympathetic nerve supply to the bladder results in incomplete emptying of the bladder during micturition, which can lead to recurrent urinary tract infections.

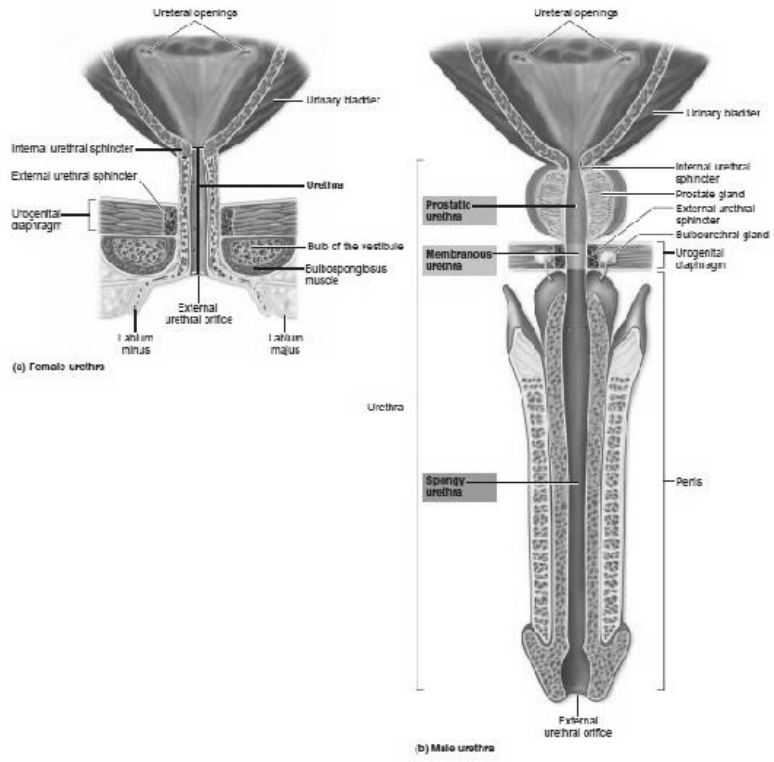
- Innervation of urinary bladder: (Fig.40)

	Parasympathetic	Sympathetic	Somatic
Origin	S 2, 3, 4	L 1, 2, 3	S 1, 2
Afferent	-Detection of degree of bladder stretch	-Sensation of fullness -Pain sensation due to overstretch	Stretch receptors in posterior urethra
Efferent	Pelvic nerve	Lesser splanchnic nerve → presacral → hypogastric nerve.	Pudendal nerve
Ganglion	Terminal	Inf. mesenteric	
Function	Contraction of wall & relaxation of internal sphincter.	Relaxation of wall & contraction of internal sphincter	Voluntary contraction or relaxation of external urethral sphincter.
Role in micturition	Essential for reflex micturition	No role It prevents semen reflux into bladder during ejaculation	Voluntary control of micturition

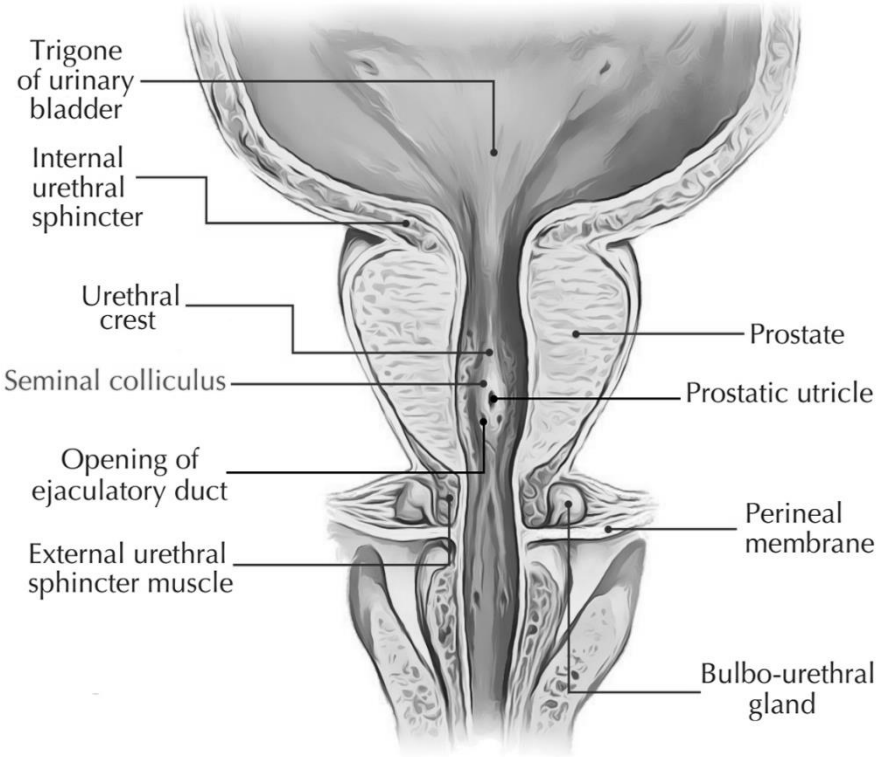


Urinary bladder and its innervation.

Fig.40



Female & male urethra



Prostatic urethra

URETHRA

MALE URETHRA

❖ S shaped, 20 cm

Parts and relations:

Preprostatic part (1 cm):

- Between the neck of the bladder and prostate
- Surrounded by internal urethral sphincter

Prostatic part: (widest part of the urethra, 3-4 cm):

- Traverses the ant part of the prostate (from its base to apex) to pelvic fascia.

Interior of prostatic urethra: the post wall shows the following:

Urethral crest: median ellipsoid elevation

Seminal colliculus (verumontanum): rounded elevation in the middle of urethral crest. It contains:

Prostatic utricle: remnants of paramesonephric ducts in males

2 ejaculatory ducts: lat to prostatic utricle.

Prostatic sinus: a groove on each side of urethral crest. It receives prostatic ducts (15-20) directly.

Membranous part (narrow part, 2 cm):

- Traverses the deep perineal pouch
- Surrounded by external urethral sphincter

Penile (spongy) part (15 cm): pierces the bulb of the penis (dilates forming bulbar fossa) → corpus spongiosum → glans penis (dilates forming navicular fossa)

External urethral meatus: (narrowest point of urethra): vertical slit at tip of glans penis.

Blood supply:

Arterial: inf vesical A, internal pudendal A &2 As of the bulb

Venous: vesical venous plexus of veins → internal iliac V.

Lymphatic drainage:

Prostatic and membranous: internal iliac lymph nodes

Penile: deep inguinal lymph nodes

FEMALE URETHRA

❖ 4-5 cm (corresponds to male urethra except the penile part)

Course:

- It is embedded in the ant wall of vagina post to retropubic fat.
- It passes from neck of bladder → deep perineal pouch (surrounded by external urethral sphincter) → superficial perineal pouch → ends by external urethral meatus in the vestibule of the vulva between the clitoris (ant) and vagina (post)

Blood supply:

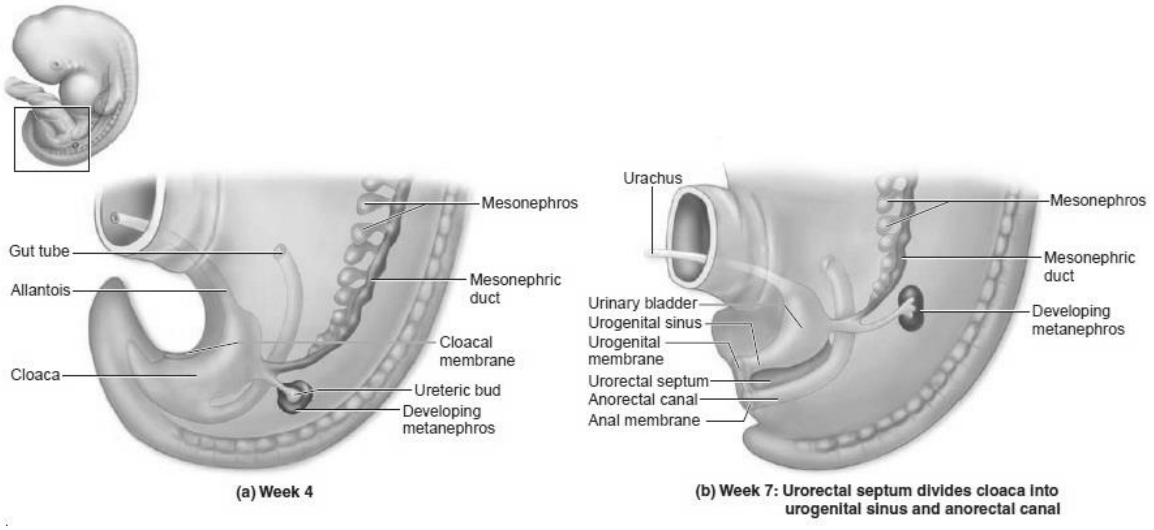
Arterial: vaginal A

Venous: vesical venous plexus of veins → internal iliac V.

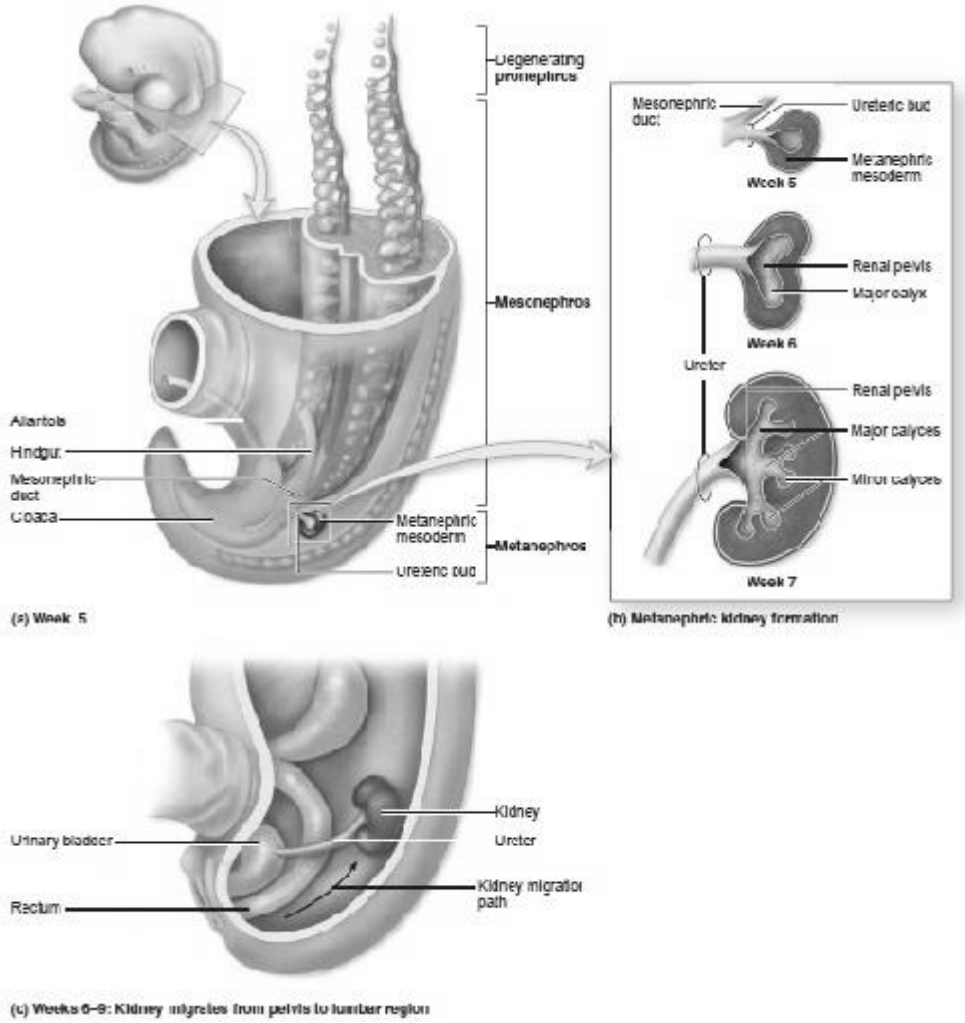
Lymphatic drainage: internal iliac lymph nodes

URETHRAL SPHINCTERS

	Internal urethral sphincter (sphincter vesicae)	External urethral sphincter (sphincter urethrae)
Site	Surrounds neck of bladder (& preprostatic urethra in males)	In deep perineal pouch
Muscles	Smooth	Skeletal
Nerve supply	Autonomic (involuntary)	Somatic (voluntary)
Functions	• Continence of urine • Prevents retrograde passage of semen (stronger in males)	Continence of urine



Cloaca



Development of kidney & ureter

URINARY SYSTEM

Development of intermediate mesoderm: it passes into three successive stages (pronephros, mesonephros and metanephros).

Pronephros: The intermediate mesoderm in the cervical region differentiates into pronephros (primitive kidney and ureter) with a formation of a pronephric duct which grows caudally to end in the primitive urogenital sinus (part of hind gut and future urinary bladder). This cervical kidney degenerates completely, the pronephric duct remains from the thoracic region downwards and is transformed into mesonephric duct.

Mesonephros: The intermediate mesoderm in the thoracic and upper lumbar region differentiates into mesonephros which attaches to the mesonephric duct. Its cranial part disappears, while the caudal part of mesonephros develops into efferent tubules of testis (in males) and degenerates in females (epoophoron and paroophoron).

***The mesonephric (Wollfian) duct*:**

- The cranial part of mesonephric duct differentiates into male genital ducts and degenerates in females.
- The caudal part of mesonephric duct gives rise to a ureteric bud and continue to end in the urogenital sinus. Both shares in the formation of urinary bladder and urethra.

- **Metanephros:** is the development of the permenant kidney.

Cloaca:

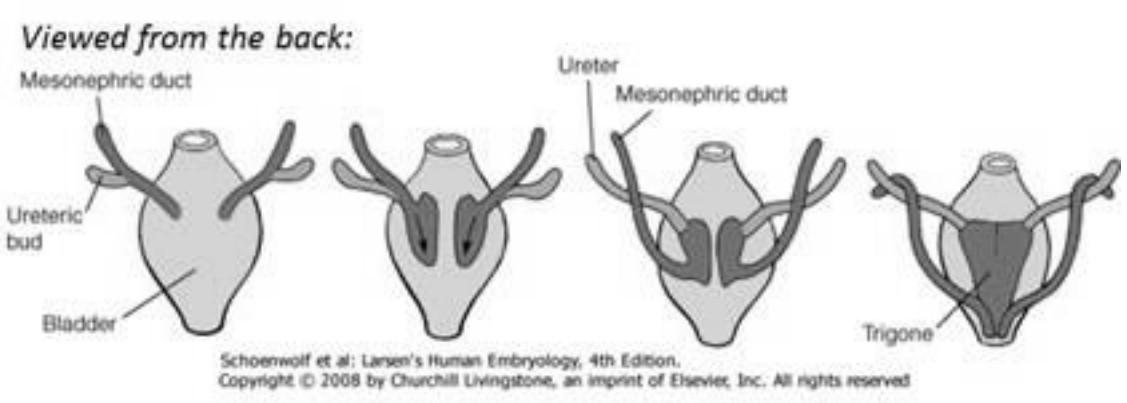
- The hindgut is connected to the yolk sac inside the umbilical cord by a diverticulum called allantois. The part caudal to the allantois is called the cloaca. The cloaca is closed caudally by cloacal membrane.
- An urorectal septum descends coronally dividing the cloaca and cloacal membrane into:
  1) ***Primitive urogenital sinus*** ventrally, closed caudally by ***urogenital membrane.***
  2) ***Anorectal canal dorsally,*** dorsally, closed caudally by ***anal membrane.***

Allantois:

- It is a diverticulum from the secondary yolk sac inside the connecting stalk. It is lined with endoderm.
- After folding it connects the hind gut (derived from endoderm) to the umbilical cord (derived from connecting stalk).
- The part connected to the hind gut will form part of the urinary bladder.
- The part extending to the umbilical cord is called the urachus which will obliterate forming median umbilical ligament connecting the urinary bladder to the umbilicus.
- It is surrounded by allantoic vessels.

Development of the kidney and ureter:

- The caudal part of the mesonephric duct gives rise to a ureteric bud.
- The ureteric bud grows cranially invading the metanephric cap (the caudal part of intermediate mesoderm in the pelvis).
- The ureteric bud forms the ureter, renal pelvis and branches to form the major calyces, minor calyces and collecting tubules.
- The metanephric cap divides forming masses over the collecting tubules called metanephric tubules.
- The metanephric tubules differentiate into distal convoluted tubules, loop of Henle and proximal convoluted tubules.



Development of urinary bladder

- The terminal part of proximal convoluted tubules is invaded by capillaries and transformed into Bowman's capsule.
- The kidney is formed in the pelvis. It ascends by the elongation of ureter to reach its normal position. As it ascends it changes its blood supply (median sacral, common iliac, aorta).

Congenital anomalies:

1) ***Renal agenesis:*** failure of metanephric cap differentiation. It may be unilateral or bilateral (fatal).
2) ***Accessory kidney, double ureter & bifid ureter:*** due to early splitting of ureteric bud.
3) ***Cystic kidney:*** due to bad connection between the collecting tubules and metanephric tubules.
4) ***Pelvic kidney:*** failure of kidney ascend.
5) ***Horse shoe kidney:*** the two kidneys fuse at their lower ends. They ascend till reaching IMA.
6) ***Accessory renal artery.***

Development of the urinary bladder:

- The trigone is formed by absorbed part of mesonephric ducts (mesodermal). Accordingly the ureters (developed from ureteric bud) open directly in the urinary bladder.
- Most of the urinary bladder is formed by the urogenital sinus (endodermal).
- The allantois contributes to the development of the apex of urinary bladder (endodermal).
- The muscular layer of the urinary bladder is formed by the surrounding splanchnic mesoderm.

Congenital anomalies:

1) ***Ectopia vesica:*** the interior of the urinary bladder is exposed directly through a defective anterior abdominal wall. It is due to defective mesoderm in between.

2) ***Urachal cyst:*** the urachus is fibrosed but a middle part of it is patent.

3) ***Urachal diverticulum:*** the part of the urachus attached to the urinary bladder is patent, the rest is fibrosed.

4) ***Urachal sinus:*** the part of the urachus attached to the umbilicus is patent, the rest is fibrosed.

5) ***Urachal fistula:*** the whole urachus is patent.

Development of the male urethra:

- The posterior aspect of the upper part of prostatic urethra is developed from mesonephric ducts (mesodermal). Accordingly the ejaculatory ducts (developed from the mesonephric duct) open in the post aspect of prostatic urethra.
- Most of the urethra develops from the urogenital sinus (endodermal). The penile urethra develops as urethral plate → urethral groove → urethral canal
- The part of the urethra traversing the glans penis is ectodermal.

Congenital anomalies:

1) ***Urethral stenosis:*** due to excessive fusion of urethral groove or defective canalization of the part traversing glans penis.

2) ***Hypospadias:*** the urethra opens in the ventral surface of penis.

3) ***Epispadias:*** the urethra opens in the dorsal surface of penis.

Development of female urethra

- The post aspect is developed from mesonephric ducts (mesodermal).
- The rest of the urethra and the vestibule is developed from urogenital sinus (endodermal).