

NEPHRON

⇒ Nepron is defined as the structure and functional unit of kidney.

- Each kidney consist of 1- 1.3 millions of Nephrons.

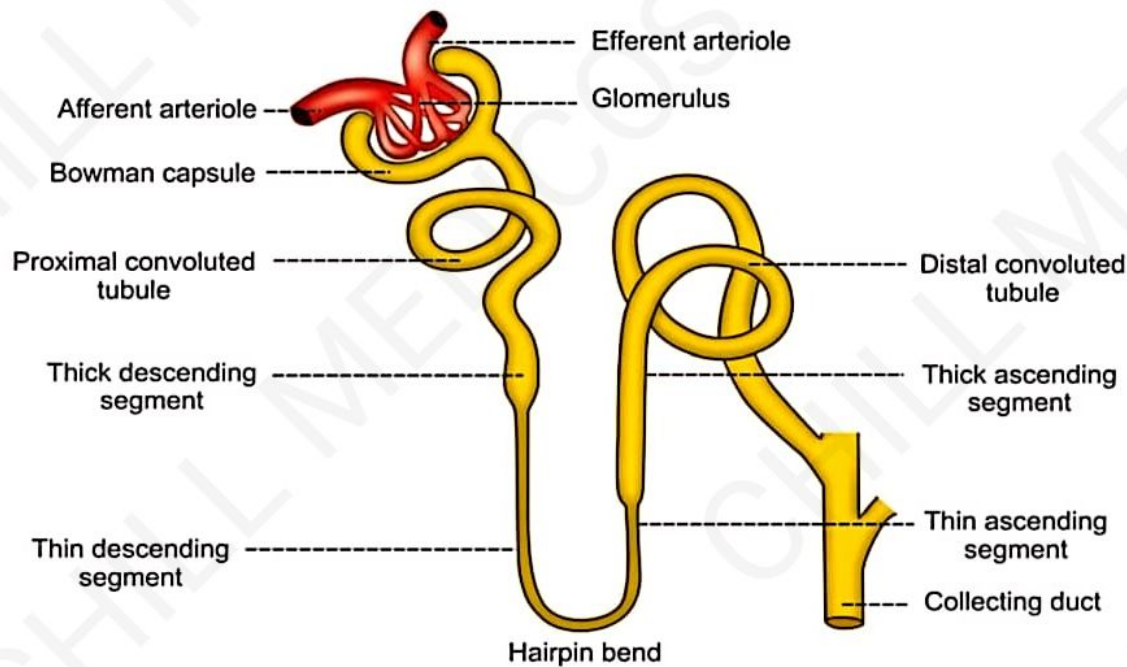


FIGURE 49.1: Structure of nephron

⇒ Each Nephron consist of two parts.

- ① Renal corpuscle / Malpighian corpuscle.
- ② Renal tubules.

1. RENAL / MALPIGHIAN CORPUSCLE

- spheroid and slightly flattened structure
- Diameter about 200 μ .

Function :- filtration of blood which form the 1st phase of urine formation.

Situation of Renal corpuscle and Types of Nephron.

- Renal corpuscle is present in the cortex of the kidney → Near → periphery
→ near the medulla.

TABLE 49.1: Features of two types of nephron

Features	Cortical nephron	Juxtamedullary nephron
Percentage	85%	15%
Situation of renal corpuscle	Outer cortex near the periphery	Inner cortex near medulla
Loop of Henle	Short Hairpin bend penetrates only up to outer zone of medulla	Long Hairpin bend penetrates up to the tip of papilla
Blood supply to tubule	Peritubular capillaries	Vasa recta
Function	Formation of urine	Mainly the concentration of urine and also formation of urine

STRUCTURE OF RENAL CORPUSCLE

- Renal corpuscle.

↓ Formed by

① Glomerulus : → tuft of capillaries.
→ consist of Afferent & Efferent Arterioles.
→ Arterioles
↓ divide
→ 4 or 5 large capillaries.

- Afferent A. → large diameter.
- Efferent A. → small diameter.

- function : — presence of fenestra cause filtration function of the glomerulus.

- ② Bowman capsule
 ↳ capsular structure, which enclose the glomerulus.

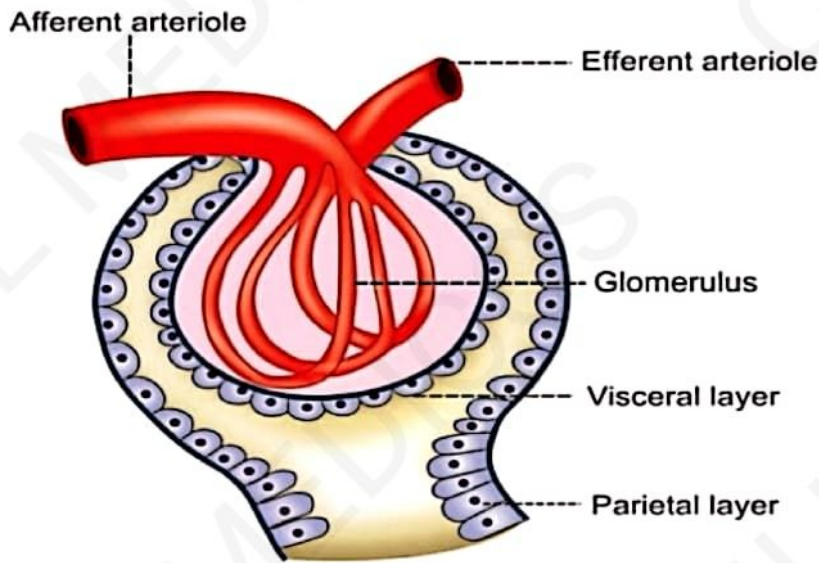


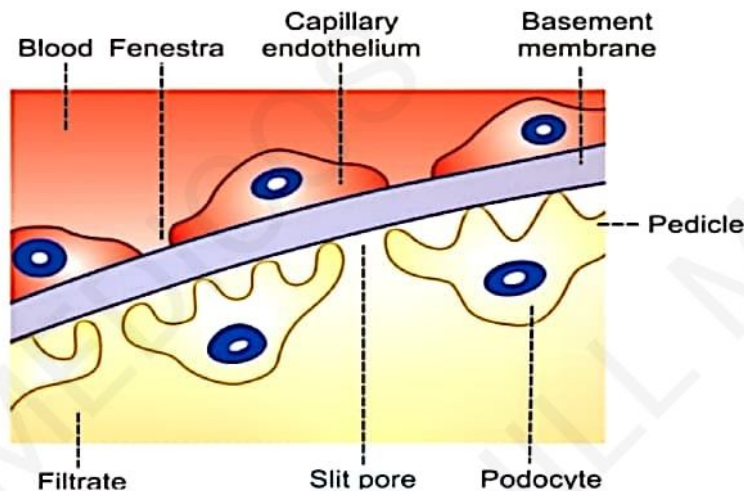
FIGURE 49.3: Renal corpuscle

→ formed by two layers.

- ① inner visceral layer
 - ② outer parietal layer.
- space b/w them continue as lumen of tubular portion

function :-
 Histological

- pedicle → cytoplasmic extension of epithelial cell.
- slit pore
 ↳ cleft b/w pedicles.
- podocytes :- [epithelial cell + pedicles]



2. TUBULAR PORTION OF NEPHRON.

- It is a continuation of Bowman capsule.

- made up of 3-parts.

① proximal convoluted tubule

② Loop of Henle

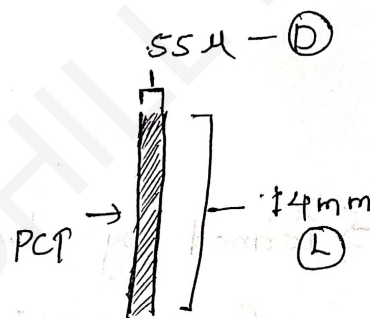
③ Distal convoluted tubule.

1. PROXIMAL CONVOLUTED TUBULE

- coiled portion arising from Bowman capsule

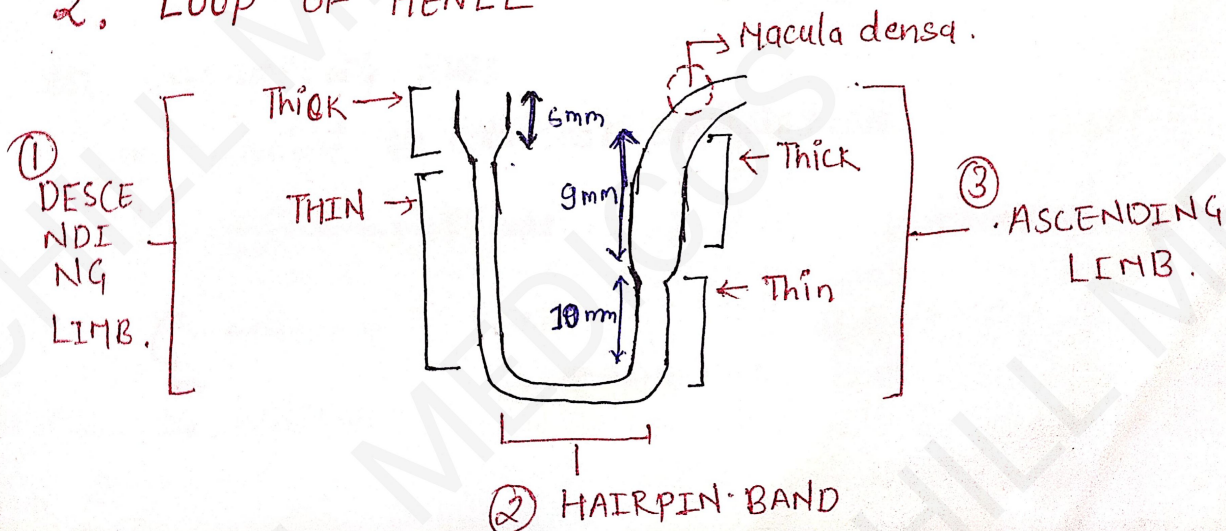
- Situated in Cortex

- continued descending limb of Loop of Henle.



- functional histology :-
 - cuboidal epithelium
 - ↳ hair like projections
 - ↓
 - Brush-Bordered cell.

2. LOOP OF HENLE



• Consist of :-

① Descending limb $\left\{ \begin{array}{l} \text{Thick} \rightarrow \text{Brush-border cuboidal E.c.} \\ \text{Thin} \rightarrow \text{flattened Epithelial cell.} \end{array} \right.$

② Hairpin Band $\rightarrow$ flattened Epithelial cell.

③ Ascending Limb $\left\{ \begin{array}{l} \text{Thin} \rightarrow \text{flattened Epithelial cell.} \\ \text{Thick} \rightarrow \text{cuboidal Epithelial cell.} \end{array} \right.$

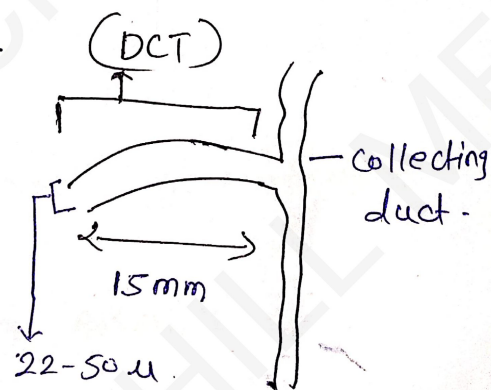
function :- concentration of urine.

③ DISTAL CONVOLUTED TUBULE.

• present in the cortex of kidney.

function:- Cuboidal E.c.
 $\downarrow$
Intercalated cell (I cells)

• Exchange of ions.



COLLECTING DUCT

• Cuboidal or columnar Epithelial cell.

$\rightarrow$ Two types of cell.

① principal or P cells

② Intercalated or I cells

JUXTAGLOMERULAR APPARATUS

- Definition :- Specialized organ situated near the glomerulus of each nephron (Juxta = Near)

STRUCTURE OF JUXTAGLOMERULAR APPARATUS

- JG Apparatus formed by.

- ① Macula densa
- ② Extraglomerular Mesangial cells
- ③ Juxtaglomerular cells.

1. Macula densa :-

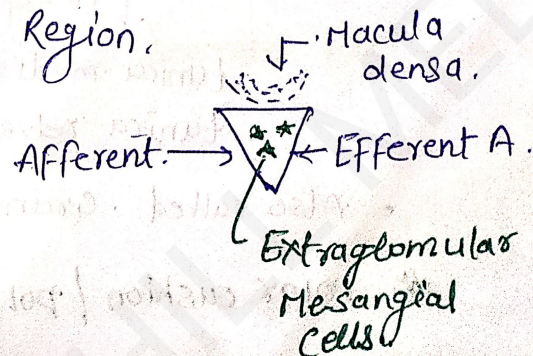
- End portion of Thick ascending segment before it opens into DCT.
- Situated b/w Afferent & Efferent Arterioles of same Nephron
- Macula densa very close to Afferent arterioles
- Formed by tight packed cuboidal epithelial cells.

2. Extraglomerular Mesangial cells.

- Situated in the triangular region.

Also called,

- agranular cells, lacis cell, Goormaghtigh cells.



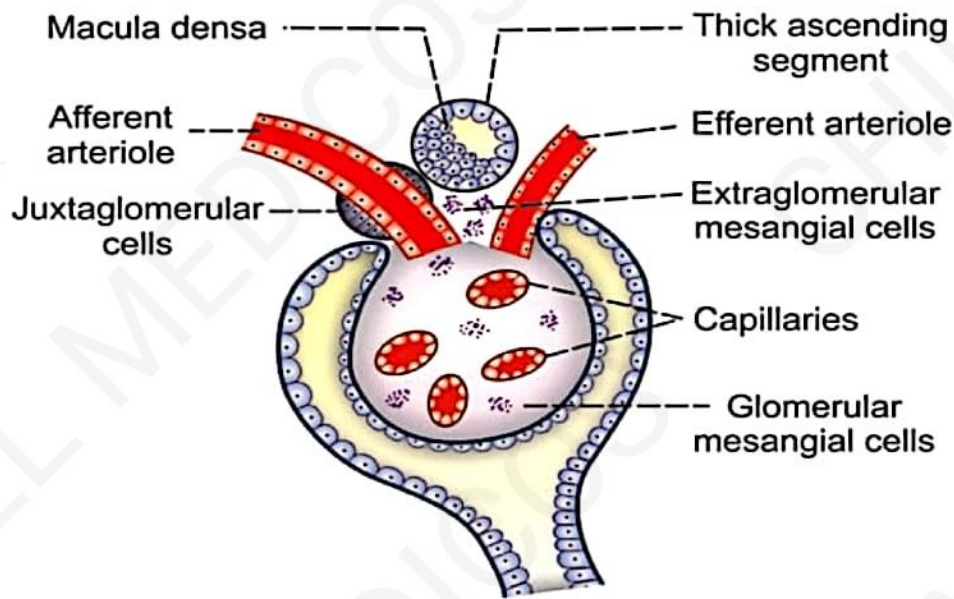


FIGURE 50.1: Juxtaglomerular apparatus

- Glomerular mesangial cells.
 - present in glomerular.
 - support the glomerular capillary loop.
 - Regulation GFR
 - ↳ By contractile properties.
 - phagocytic → Re.
 - secrete glomerular matrix, prostaglandins, cytokines.

3. Juxtaglomerular cells.

⇒ specialized smooth muscle cells. situated in the wall of afferent arterioles. Just before Enter Bowman capsule.

- smooth muscle cell

↓ Mostly present

tunica media

tunica adventitia.

] - A.A.

- Also called Granular cells. [secretory granules]

Polar cushion / polkissen.

FUNCTIONS OF JUXTAGLOMERULAR APPARATUS

①. SECRETION OF HORMONES.

↳ JG Apparatus. secretes two hormones.

1. Renin
2. prostaglandin.

1. Renin:-

- Juxtaglomerular cell secrete → Renin
- peptide with 340 AA

Along with Angiotensins Renin forms.

↓
RENIN-ANGIOTENSIN SYSTEM.

↳ Maintenance of B.P.

- secretion of Renin stimulate by

① fall in arterial B.P.

② ↓ in ECF volume

③ ↑ sympathetic activity.

④ ↓ load of Na & chloride in macula densa.

2. prostaglandin:

- Extraglomerular mesangial cell. → secrete prostaglandin

⇒ Note# Interstitial cell [Medulla]

(Type-I M.I.C) ↳ Also secrete prostaglandin

2. SECRETION OF OTHER SUBSTANCES.

- Extraglomerular Mesangial cells $\xrightarrow{\text{secrete}}$ cytokines like:
 - Interleukin - 2
 - Tumor necrosis factor.
- Macula densa $\longrightarrow$ Thromboxane A_2 .

3 REGULATION OF GLOMERULAR BLOOD FLOW & GFR

- Macula densa $\longrightarrow$ tubuloglomerular feedback.

$\downarrow$ Regulate

GFR & GBF

RENIN - ANGIOTENSIN SYSTEM

- ~~Renin~~ α_2 -globulin. - [Angiotensin]
↓ substrate for
Renin.

* Angiotensin - I [decapeptide]

* Angiotensin - II [octapeptide] → Half life - 1-2 minute

* Angiotensin III [heptapeptide]

* Angiotensin - IV [hexapeptide]

Enzymes :-

1. Angiotensin converting Enzyme [ACE]

→ convert Angiotensin I → Angiotensin II
→ secreted from lungs.

2. Angiotensinase :

→ convert Angiotensin II → Angiotensin - III
→ present RBC & vascular bed in many tissue.

ACTIONS OF ANGIOTENSINS.

1. ANGIOTENSIN - I

→ physiological inactive.
→ serve only precursor.

2. ANGIOTENSIN - II

→ Most Active form.

* Actions on :-

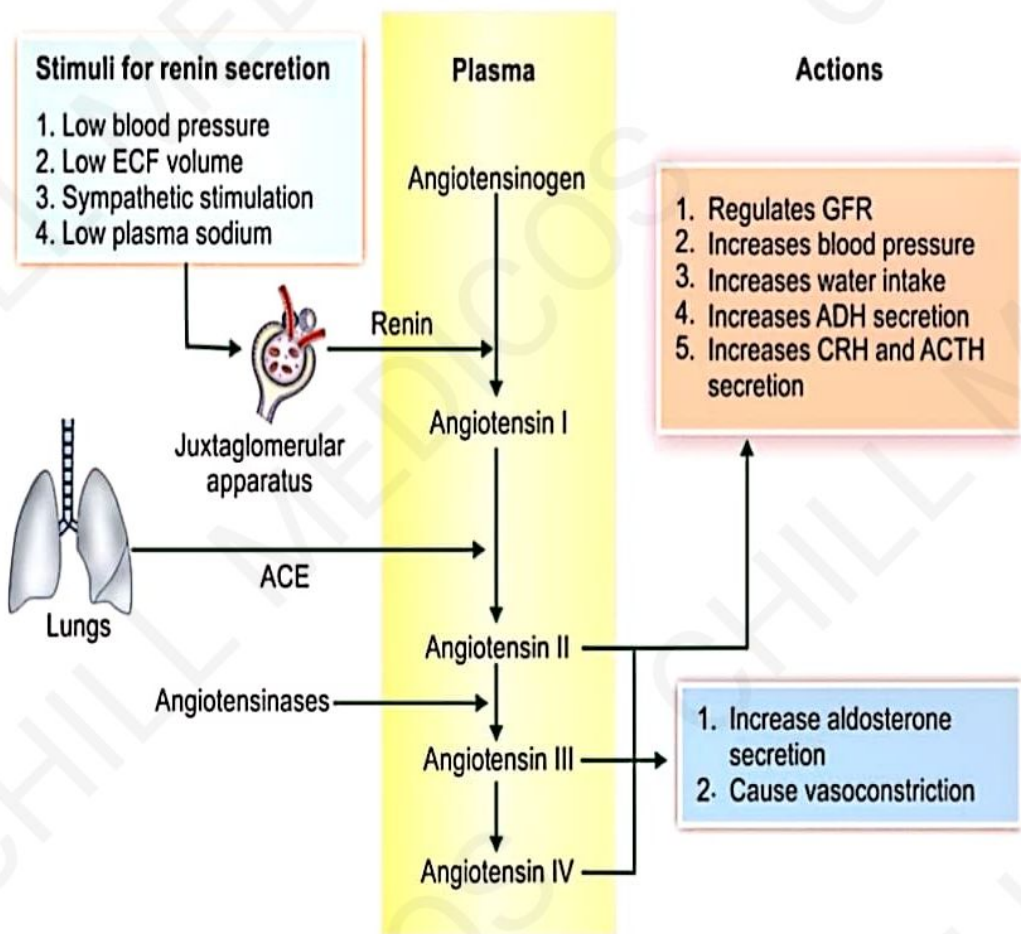


FIGURE 50.2: Renin-angiotensin system. ECF = Extracellular fluid, ACE = Angiotensin-converting enzyme, GFR = Glomerular filtration rate, ADH = Antidiuretic hormone, CRH = Corticotropin-releasing hormone, ACTH = Adrenocorticotrophic hormone.

[a] on Blood vessels

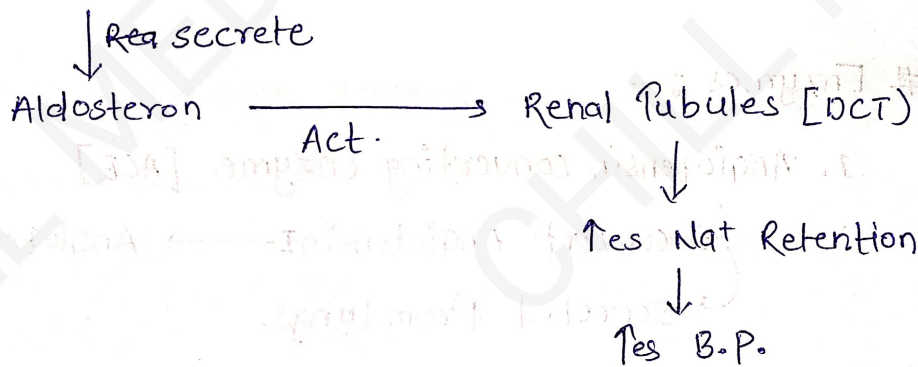
Vasoconstriction

- potent constrictor of Arterioles
- ↑ B.P.
- It is Hypertensin

Indirect ↑ B.P by Release → noradrenaline (vasoconstrictor)
postganglionic Gang Sympathetic fiber

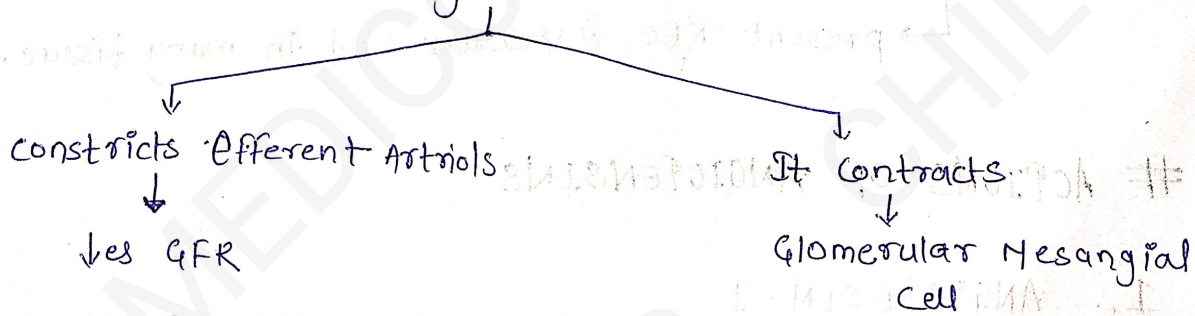
[B] on Adrenal cortex

- stimulate Zona Glomerulosa



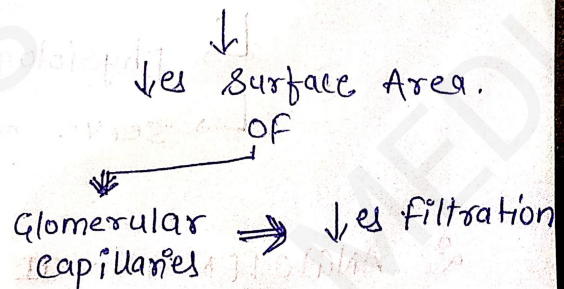
[C] on Kidney.

- Angiotensin-II Regulated GFR



NOTE :- Initial ↑ GFR

- ↑ Not Reabsorption from Renal tubules (DCT)



[d] on Brain

- Inhibit - Baroreceptor Reflex $\rightarrow$ $\downarrow$ BP
- $\uparrow$ water intake by stimulate thirst center.
- $\uparrow$ secretion of $\rightarrow$ CRH [Hypothalamus]
 - $\rightarrow$ $\uparrow$ secretion of ACTH [pituitary]
- $\uparrow$ secretion of
 - $\downarrow$
 - ADH [Hypothalamus]

3. ANGIOTENSIN - III

- $\uparrow$ B.P.
- stimulates aldosterone secretion from adrenal cortex.
 - $\rightarrow$ 100% Adrenocortical stimulation Activity
 - $\rightarrow$ 40% vasopressor activity of angiotensin-II.

4. ANGIOTENSIN - IV

- $\rightarrow$ also has Adrenocortical stimulation and vasopressor activities.

GLOMERULAR FILTRATION RATE [GFR]

- GFR defined as the Total quantity of filtrate formed in all the nephrons of both the kidneys in the given unit of time.
- Normal GFR is 125 mL/minute or 180L/day.
- Its constituent is same as plasma except glomerular filtrate doesn't have plasma protein and cells.

$$GFR = K_f [P_{gc} - P_{bs}] - [\pi_{gc} - \pi_{bs}]$$

K_f = filtration coefficient

P_{gc} = Glomerular capsule hydrostatic pressure
= 40 mm Hg

P_{bs} = Bowman's capsule hydrostatic pressure
= 10 mm Hg

π_{gc} = Glomerular capsule osmotic pressure
= 20 mm Hg

π_{bs} = Bowman's capsule osmotic pressure
= 0 mm Hg

$$\begin{aligned} GFR &= 12.5 [40 - 10] - [20 - 0] \\ &= 12.5 [30] - [20] \\ &= 12.5 [30 - 20] \\ &= 125 \text{ mL/min} \end{aligned}$$

$$\# \text{ Filtration fraction} = \frac{\text{GFR}}{\text{Renal plasma flow}} \times 100$$

$$\text{Normal} = 19.2\%$$

$$\# \text{ Net filtration pressure} = \text{Glomerular capillary pressure} - \text{Colloidal osmotic pressure} + \text{Hydrostatic pressure in Bowman capsule.}$$

$$= 60 - (25 + 15) = 20 \text{ mm Hg}$$

$$\# \text{ Filtration coefficient} = \frac{\text{GFR}}{\text{Net filtration pressure}}$$

$$= \frac{125 \text{ mL}}{20 \text{ mm Hg}} = 6.25 \text{ mL/mm Hg}$$

FACTORS REGULATING (AFFECTING) GFR.

① Renal Blood Flow.

* $\text{GFR} \propto \text{Renal Blood Flow}$

↳ Autoregulated.

② Tubuloglomerular feedback.

↳ Mechanism regulate GFR by — Renal tubules
↳ Macula densa.

• Macula densa

↳ detects the sodium chloride concentration

①

↑ in GFR



↑ in NaCl concentration
in Renal tubule



Macula densa



ATP → ^{3P_i} Adenosine



Constriction of Afferent
Arteriole



↓ in ~~GFR~~ Glomerular
Blood Flow

↓ in GFR.



↑ Tubuloglomerular
feedback

When con. of NaCl ↑ in filtrate

②

↓ in GFR



↓ in NaCl con.
in Renal tubule



Macula densa



PGE₂
Bradykinin

Renin

Angiotensin

Form

Angiotensin-II

dilation of
Afferent Art.

Constriction of
Afferent Arte



↑ in GFR

When con. of NaCl ↓ in filtrate



#

Tubuloglomerular feedback sensitivity

↑ by
 → Adenosine
 → Thromboxane
 → PGI_2

↓ by.
 → Atrial Natriuretic Peptide (ANP)
 → prostaglandin I_2
 → cAMP

③ Glomerular capillary pressure

$GFR \propto \text{Glomerular capillary pressure}$

↳ Normal = 60 mmHg
 ↳ depend on → Renal blood flow
 ↳ Arterial blood P.

④ Colloidal osmotic pressure

$GFR \propto \frac{1}{\text{colloidal osmotic pressure}}$

↳ Normal = 25 mmHg.

↓
 ↑ by → dehydration
 ↓ by → Hypoproteinemia.

⑤ Hydrostatic pressure in Bowman capsule

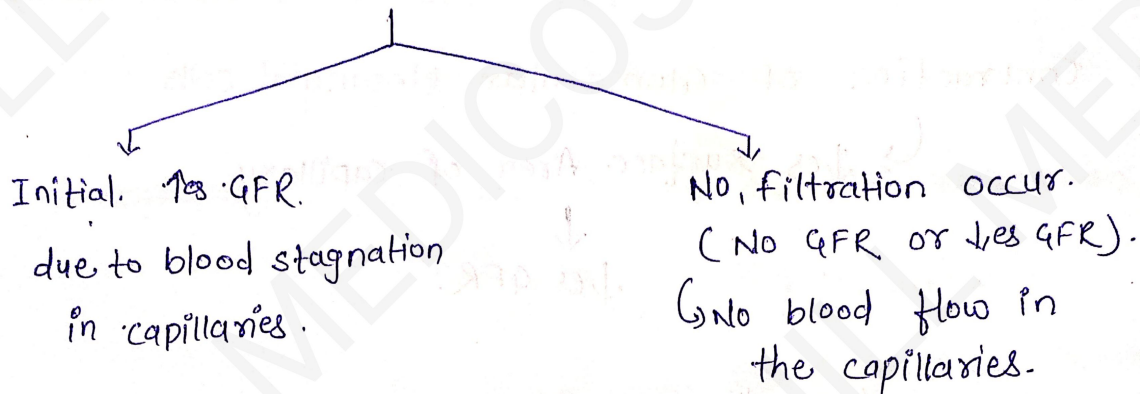
$GFR \propto \frac{1}{\text{Hydrostatic pressure in Bowman capsule}}$

↳ ↑ in → obstruction in urethra
 ↳ edema of kidney beneath Renal capsule

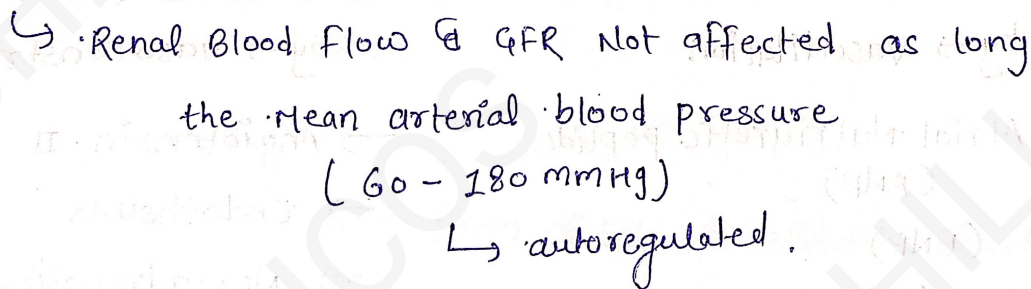
⑥ Constriction of Afferent Arteriole



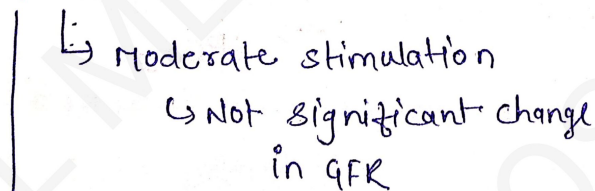
⑦ Constriction of Efferent Arteriole



⑧ Systemic Arterial pressure

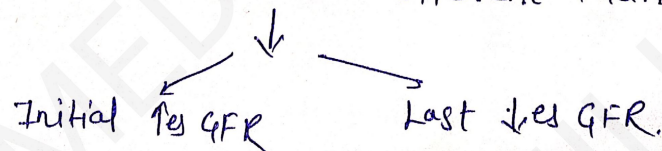


⑨ Sympathetic stimulation

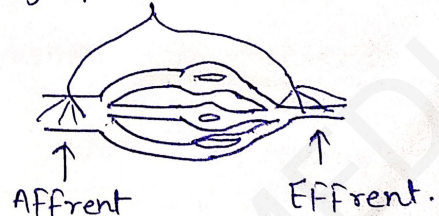


↳ Strong stimulation.

↳ Severe constriction on Efferent than Afferent



Sympathetic Nerve



⑩ Surface area of capillary membrane

$GFR \propto \text{surface A. of capillary M.}$

⑪ permeability of capillary membrane

$GFR \propto \text{permeability.}$

⑫ Contraction of Glomerular Mesangial cells

↳ ↓ surface Area of capillary

↓
↓ GFR.

⑬ Hormonal and other factors.

* Factors ↑ GFR

by → vasodilation

→ Atrial Natriuretic peptide (ANP)

→ (BNP)

→ cAMP

→ Dopamine

→ PGE_2

* Factors ↓ GFR

by → vasoconstrictor.

→ Angiotensin - II

→ Endothelins

→ Nor-adrenaline

→ Platelet-activating factor

→ PGF_2

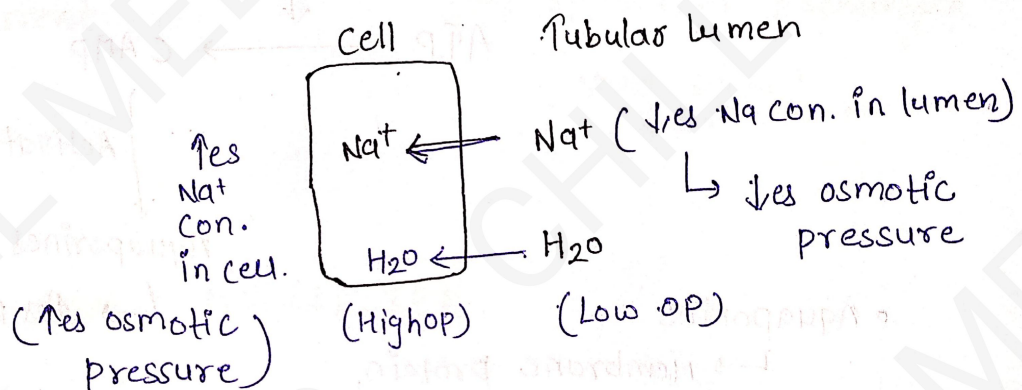
REABSORPTION OF WATER

- Reabsorption of H_2O occurs
 - PCT
 - DCT
 - collecting duct.

1. Reabsorption of water $\rightarrow$ PCT

$\rightarrow$ obligatory water reabsorption

$\Rightarrow$ Reabsorption of water depend on Na Reabsorption.



2. Reabsorption of water from distal convoluted tubule

(DCT) and collecting duct $\rightarrow$ facultative water reabsorption.

$\rightarrow$ facultative reabsorption

• Normal.

DCT + collecting duct.

(impermeable to H_2O)

• when ADH present

$\rightarrow$ DCT + collecting

duct
 $\downarrow$

Permeable to
 H_2O .

Mechanism of Action of ADH - Aquaporins.

- ADH $\uparrow$ H_2O Reabsorption in DCT & CT

↓ stimulating.
water channels (Aquaporins)

ADH $\xrightarrow{\text{combine}}$ Vasopressin (V_2) Receptors

↓ Activate
Adenyl cyclase

ATP $\longrightarrow$ CAMP

↓ Activates.
Aquaporins.

↳ $\uparrow$ H_2O Reabsorption.

- Aquaporins

↳ Membrane protein,

↳ function as water channel.

- In Mammals $\rightarrow$ 10 Aquaporins identify

↓
5 Aquaporins found in Humans.

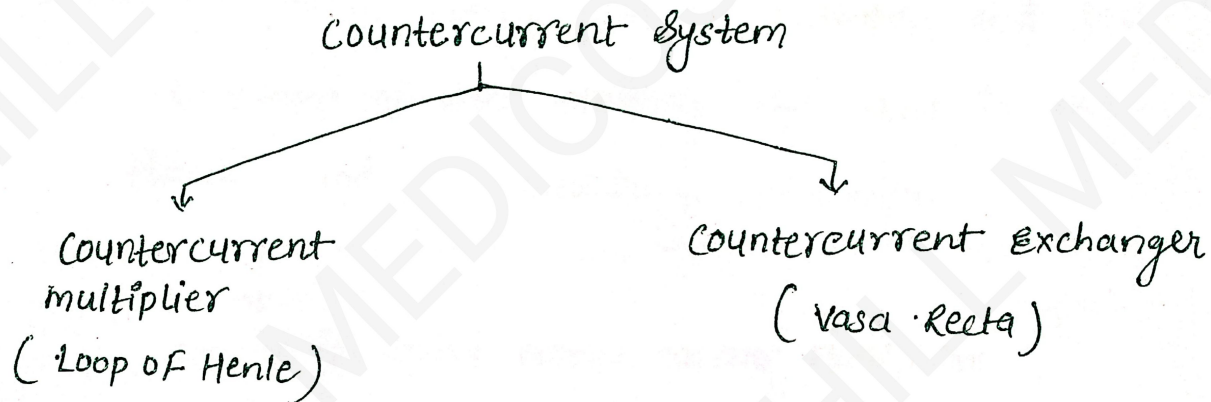
Aquaporine - 1, 2, 3 $\rightarrow$ present in Renal Tubules
↳ form H_2O channel in Renal tubules.

Aquaporine - 4 $\rightarrow$ present in Brain

Aquaporine - 5 $\rightarrow$ present in salivary gland

COUNTERCURRENT MECHANISM

- System of U-shaped tubules (tube) in which, the flow of fluid in opposite direction in two of limb of the U-shape tubules.



1. COUNTERCURRENT MULTIPLIER.

Loop of Henle

↳ Responsible for development of Hyperosmolarity of medullary interstitial fluid and medullary gradient.

Role of Loop of Henle in development of medullary Gradient.

↳ Juxtamedullary Nephron play major Role.

↳ Because loop of Nephron is long and extended in deeper part of medulla.

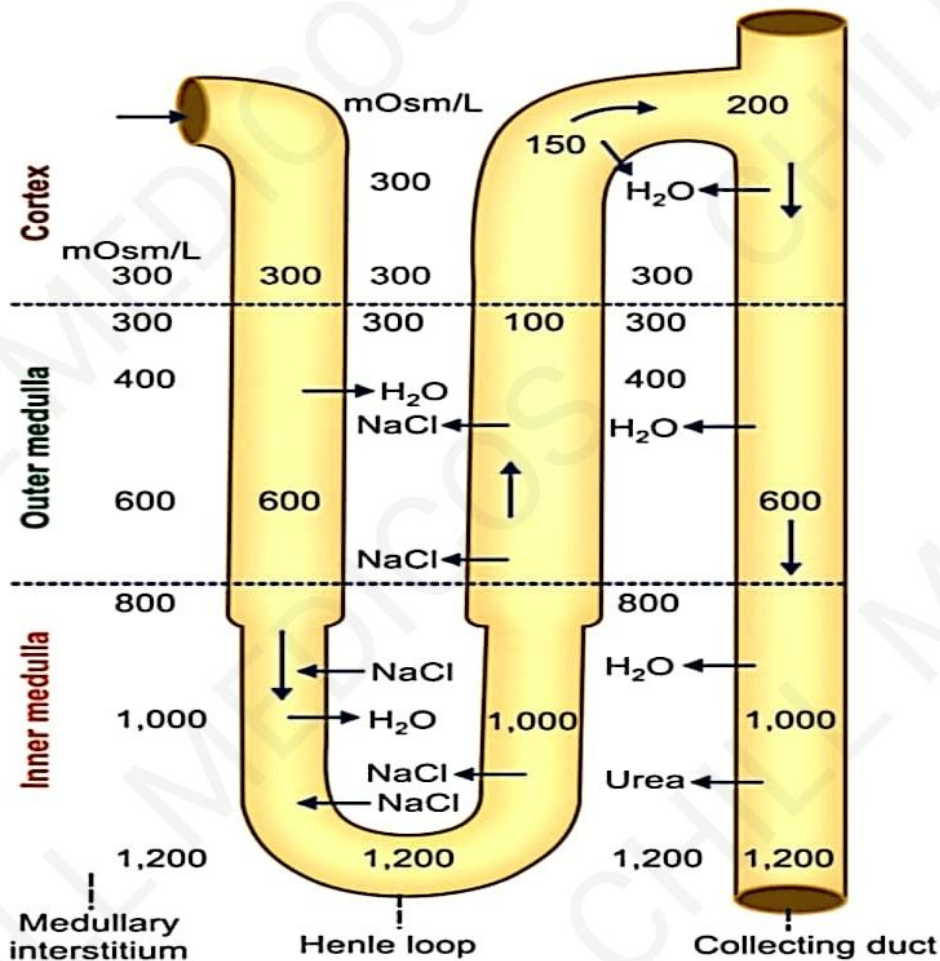


FIGURE 53.1: Countercurrent multiplier.
Numerical indicate osmolarity (mOsm/L)

• Hyperosmolarity of medulla interstitial fluid

due to $\rightarrow$ Active Reabsorption of NaCl and other solute $\rightarrow$ from Ascending limb of Henle

solute Accumulate in Medullary interstitial fluid $\rightarrow$ $\uparrow$ osmolarity
 $\downarrow$ due to it.

$\uparrow$ conc. gradient of NaCl in medullary space.

$\downarrow$ ions diffused into.

NaCl by Hairpin loop.

from Blood NaCl $\rightarrow$ descending limb of Henle.

* The sodium and chloride ions are repeatedly re-circulated b/w ascending and descending limb of Henle through medullary interstitial fluid and small portion of NaCl excreted.

↳ Due to more adding NaCl in filtrate and less excretion of NaCl multiply the NaCl in the filtrate and $\uparrow$ medullary osmolarity.

↓
So, it is called countercurrent multiplier.

Other factors responsible for hyperosmolarity of medullary interstitial fluid.

(i) Reabsorption of sodium from collecting duct.

• Collecting duct
(Medullary part)

(Medullary interstitial fluid)
Na⁺ → $\uparrow$ Na⁺ → $\uparrow$ osmolarity

(ii) Recirculation of urea.

• Collecting duct is impermeable to urea

However, DCT & CT reabsorb H₂O → by action of ADH
↓
conc of urea $\uparrow$ in DCT & CT.

* due to conc. gradient urea diffused from CTD
to (inner medullary part) into medullary
interstitium.

* urea recirculation accounts for 50% of Hyper-
osmolarity in inner medullary space.

* urea transporters :- UT-A₁, UT-A₃

↓ Activated by
ADH

2. COUNTERCURRENT EXCHANGER.

☐ Vasa Recta

↳ Responsible maintenance of medullary gradient.

Role of Vasa Recta in the Maintenance of Medullary
Gradient.

• vasa recta acts like counter current exchanger.
because of its position

• Vasa Recta

- descending limb $\xrightarrow{\text{Run with}}$ Ascending limb of Henle loop
- Ascending limb $\xleftarrow{\text{Run along}}$ descending limb of Henle loop

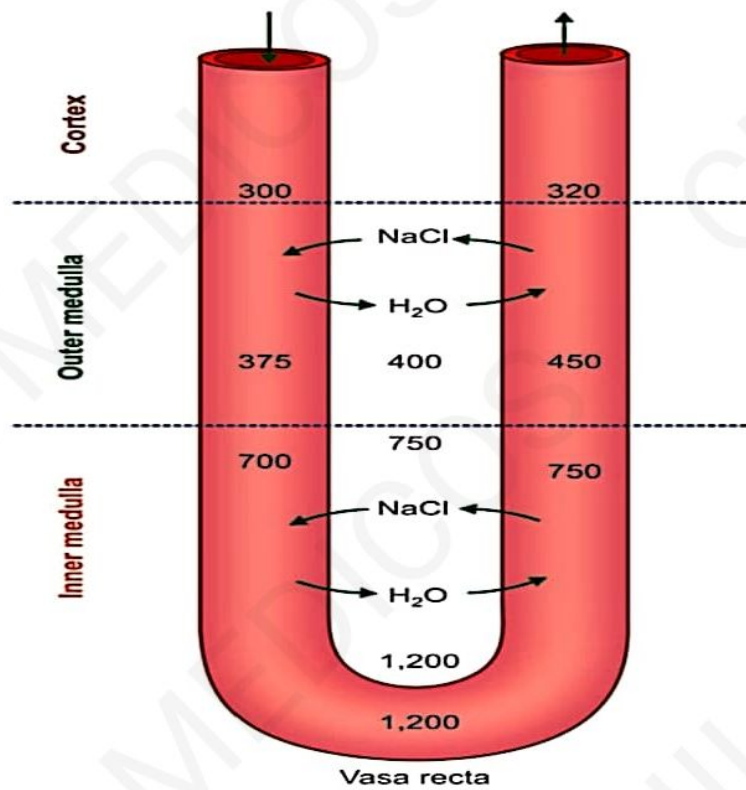
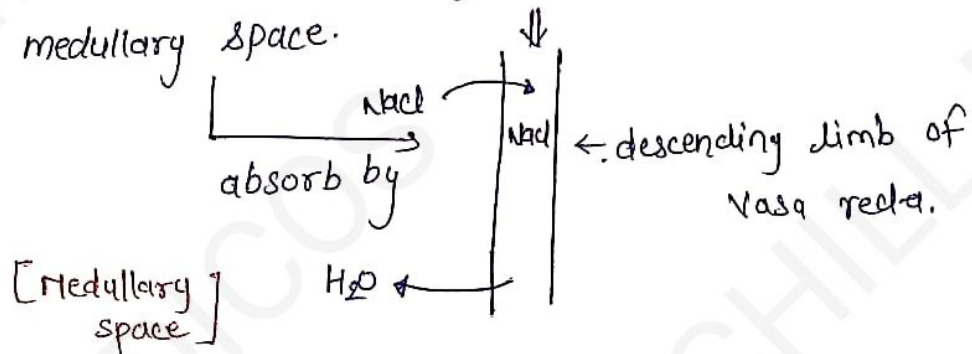


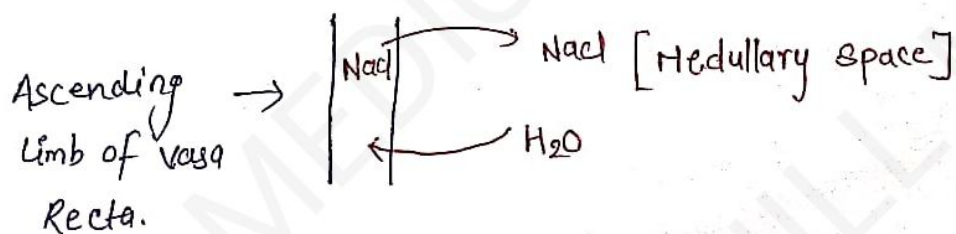
FIGURE 53.2: Countercurrent exchanger. Numerical indicate osmolarity (mOsm/L)

- Reabsorption of NaCl from Ascending limb of Henle Enter to medullary space.



due to slow blood flow from descending limb of Vasa Recta collect more NaCl and Riches

to. Ascending limb of vasa Recta by
the Hairpin loop (U)



These cycle is Repeated and maintain medullary gradient.

Vasa Recta Retains NaCl in the medullary interstitium and Removes water from it. so, the Hyperosmolarity of medullary interstitium is maintained..

Recycling of urea also occurs through vasa recta.

MICTURATION REFLEX

- This Reflex elicited by the stimulation of stretch Receptors on the wall of urinary bladder and urethra

- 300-400mL of urine is collected in bladder

↓
Intravesical pressure ↑

↓
stretched bladder

↓
stimulation of stretch receptors

↳ Generation of nerve impulse

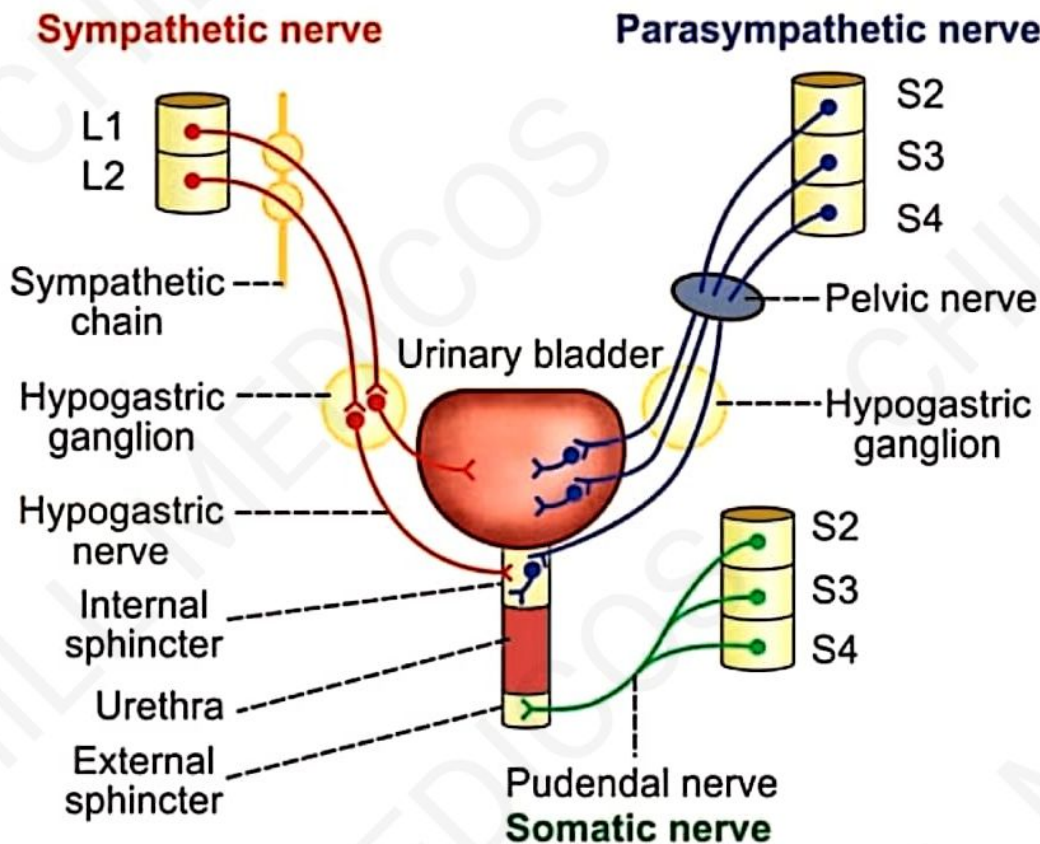
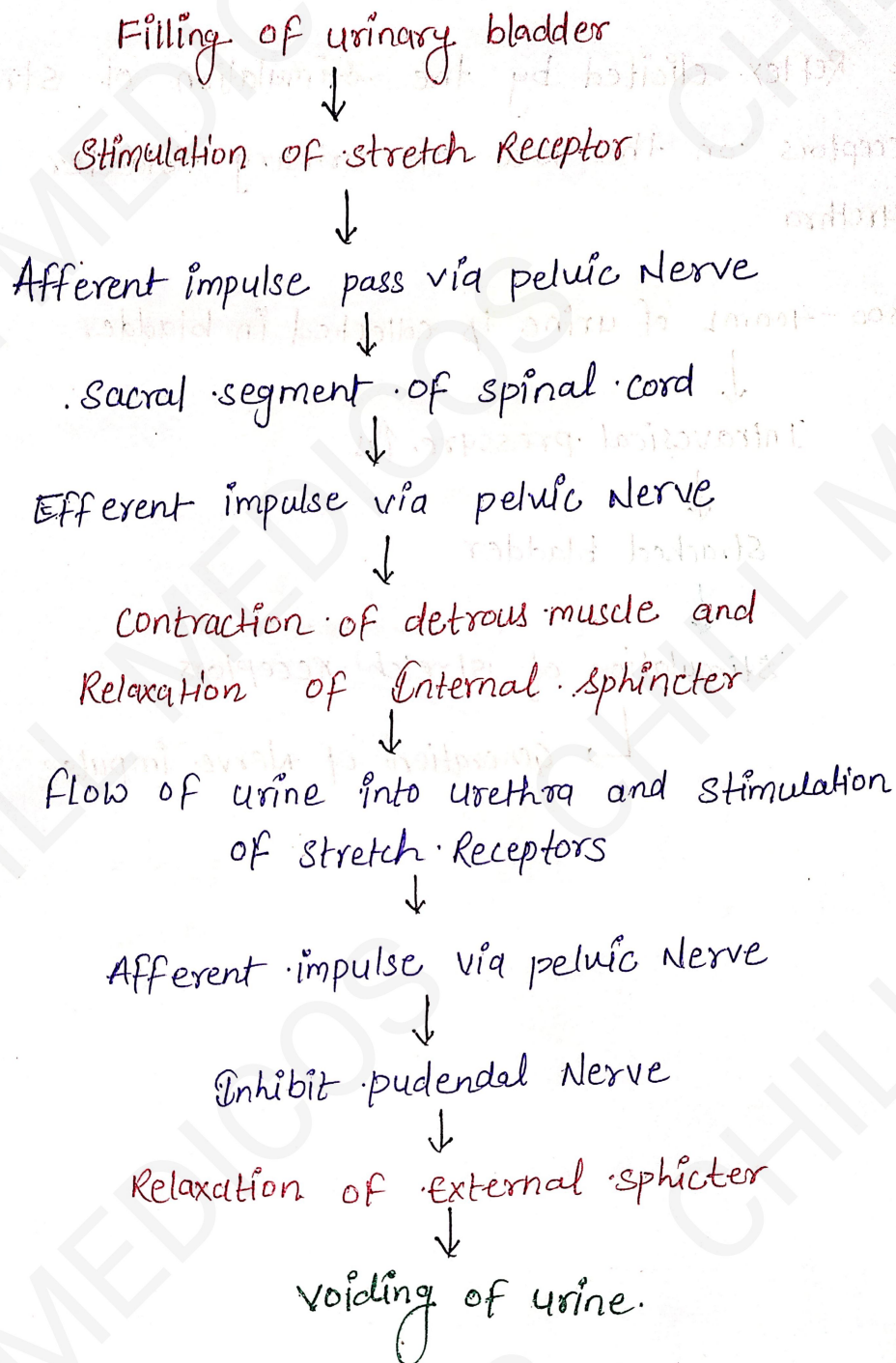


FIGURE 57.3: Nerve supply to urinary bladder and urethra

pathway of Micturition Reflex



- once Micturition Reflex begins it is self-regenerative
- Initial contraction of bladder further activates the receptor
 - ↓
 - still further increases the sensory impulse from bladder and urethra.
- These cycle continue until the force of contraction of bladder reaches maximum.

* Voided. The urine voided out completely

⇒ During Micturition the flow of urine is facilitated by the abdominal pressure.

Higher centers for micturition.

- Spinal centers
 - Sacral Region
 - Lumbar segment.

* Spinal centers Regulated by Higher centers.

Inhibitory centers
for micturition

- Midbrain
- Cerebral cortex

Facilitatory centers
for micturition

- Pons
- Some center in Cerebral cortex

Applied physiology

- ① Atonic bladder → destruction of sensory N. fiber.
- ② Automatic bladder → Hyperactive micturition Reflex
- ③ Nocturnal micturition → involuntary voiding of urine during night.