Kidney

المحاضرة الأولى

بتاريخ ١٥ فبراير ٢٠١٨

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"KIDNEY"

Functions 3 2 1 — Major **HOMEOSTATIC** function

- Regulation of
  - H_2O and electrolyte balance
  - Acid base balance ← excretion of acids, buffers, NH_3
  - ABP — short term: Renin Angiotensin II; long term: Plasma volume
- Excretion of
  - endogenous: Metabolic waste products — urea, uric acid, creatinine, bilirubin, Hormones
  - exogenous: Foreign chemicals — e.g drug, food additives
- Endocrinal Function (هرمونيا) ← Erythropoietin 85%, 1,25 $(OH)_2$ CC, Renin
- Paracrinal function ← PGE_2 PGI_2, Bradykinin
- Gluconeogenesis — in fasting

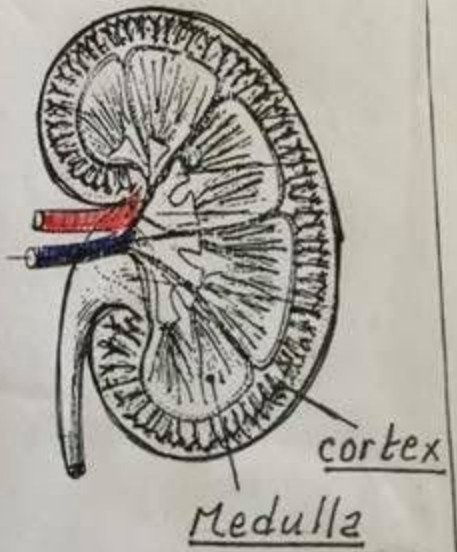
Physiologic anatomy

Weight : 150 gm
Size : Clinched fist
< 12cm × < 8 cm

Two major regions :
- Cortex granular deeper
- Medulla striater paler

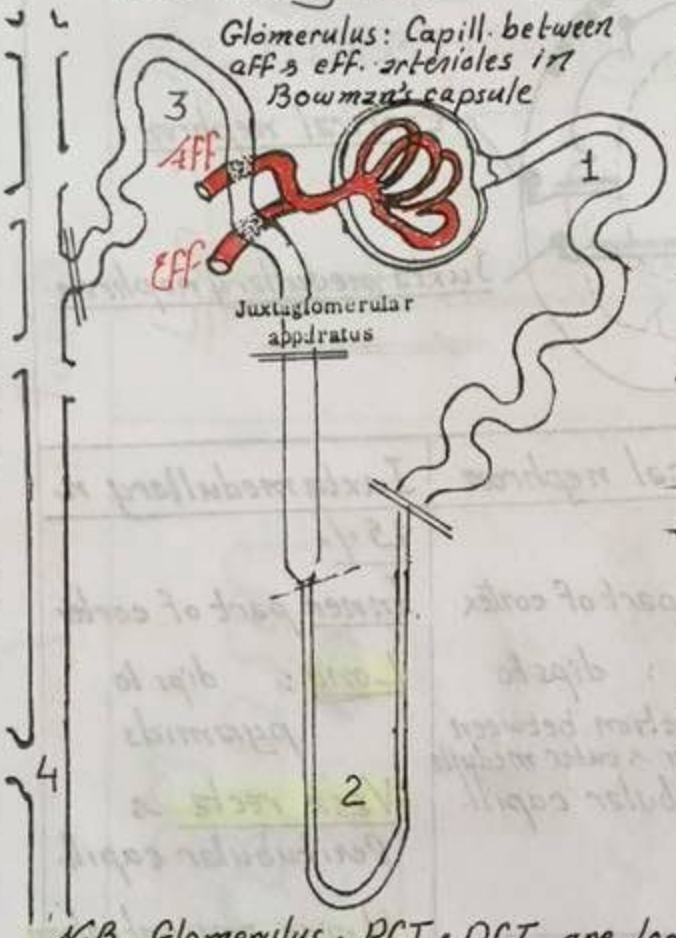
" is divided into pyramids
pyramid → renal papilla
→ minor calyx → major calices
→ pelvic → ureter

N.B Calyces, pelvis & ureter have smooth muscles



Microscopic anatomy

Each kidney contains 1.3 million **nephron** — Functional unit: Glomerulus, Tubule



1. **PCT** — single layer, 15 mm
   Apex: tight junction, brush border, more mitoch, lateral interceh space

2. **Loop of Henle**
   - Thin: flat epith — Descending & ½ ascend
   - Thick: Cuboidal cells.

3. **DCT** — 5 mm
   No bruch border, few microvilli, Less Mitochondria

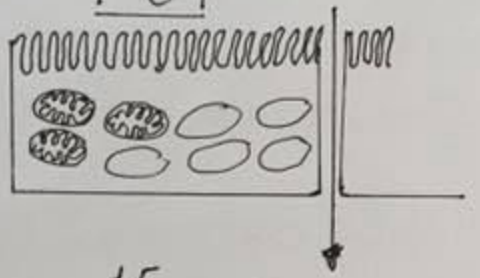
4. **Collecting T.** — 20 mm
   2 types of cells — P, I

N.B Glomerulus, PCT & DCT are located in renal cortex

Principal cells **P** cells	Intercalated cells **I** cells
(1) Predominal cells	Less number
(2) Less microvilli, mitochondria, vesicles	More
(3) Functions - Na^+ - K^+ exchange via aldosterone - H_2O reab ADH	Functions - Acid secretion - HCO_3^- reabsorption.

Nephron 1.3 M Glomerulus + Tubule

PCT

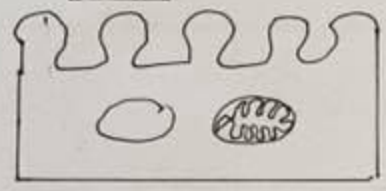


15 mm

Brush border

Many Mitoch

DCT

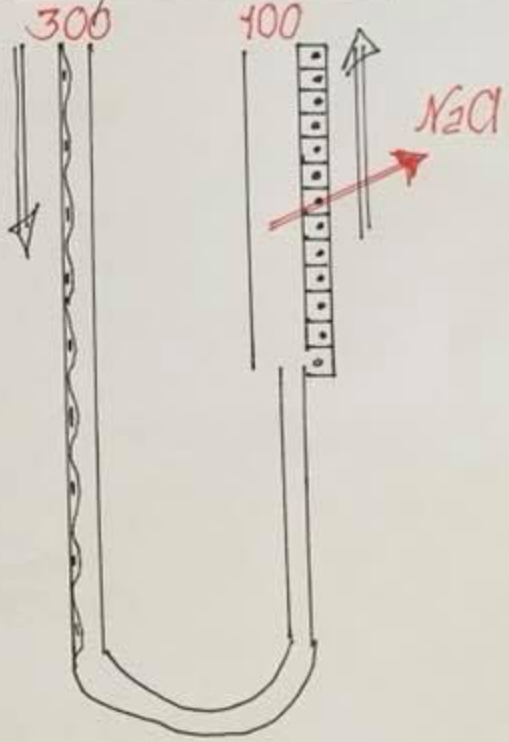


5 mm

Few Microvilli

Few Mitochondria

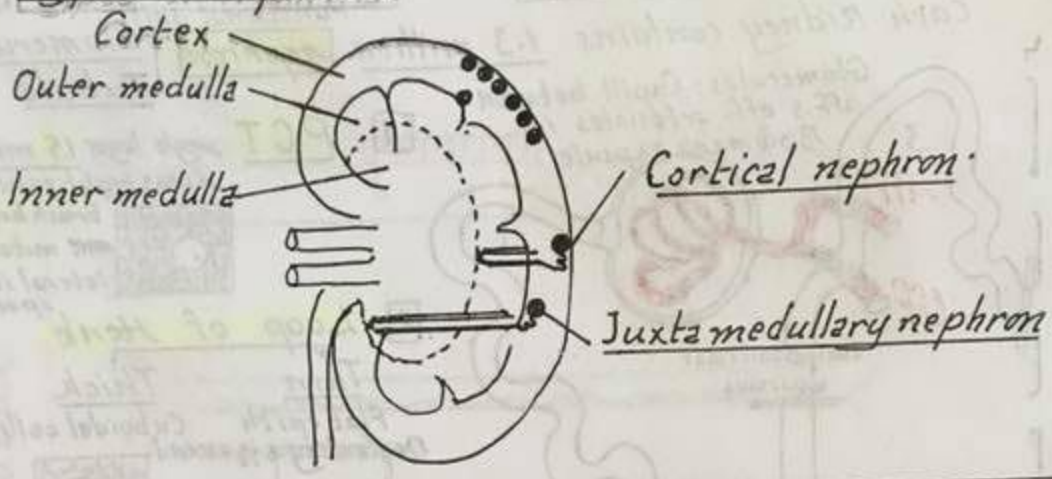
Loop of Henle



Collecting tubule

Principal cells P cells	Intercalated cells I cells
① Predominal cells	① Less number
② Less microvilli mitochondria vesicles	② More
③ Functions	
- Na-K exchange Aldosterone	③ Acid secretion
- H_2O reab ADH	HCO_3^- reabsorption

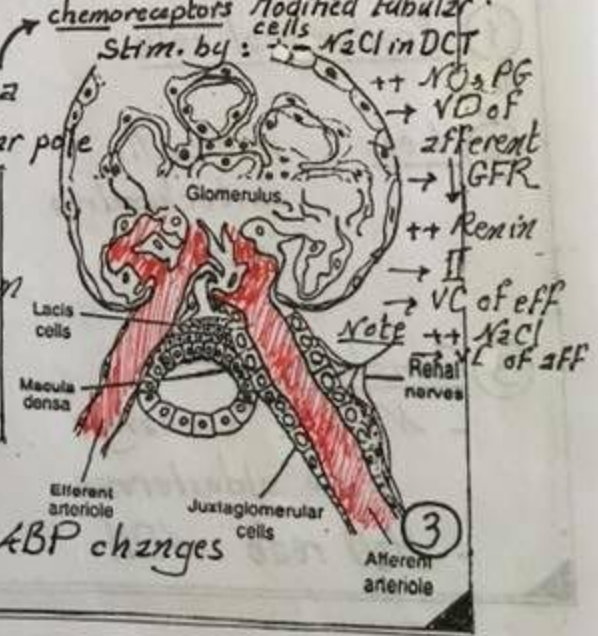
Types of nephrons



	Cortical nephron	Juxtamedullary n.
1 % of total	85 %	15 %
2 Glomerulus	Outer part of cortex	Inner part of cortex
3 Loop of Henle	Short : dips to junction between inner & outer medulla	Long : dips to pyramids
4 Blood supply	Peritubular capill.	Vasa recta & Peritubular capill.
5 Specific function	———	Urine concentration

Juxta glomerular apparatus

Area of contact between
- Distal tubules: 1st part: Macula densa
- Aff & Eff arterioles: At vascular pole



baro-receptors

Juxtaglom. cells	Lacis cells
1 Granular	Agranular
2 Media of afferent arteriole	Junction between aff & eff arterioles
3 Secrete renin	Stores renin

Function: Autoregulation of GFR & RBF with ABP changes of same nephron.

Types of nephrons

	Cortical nephron	Juxta medullary nephron
① % of total	85 %	15 %
② Glomerulus	Outer part of cortex	Inner part of cortex
③ Loop of Henle	Short dips to junction between inner & outer medulla	LONG dips to pyramid
④ Blood supply	Peritubular capill.	Peritubular capill VASA RECTA
⑤ Specific function		Urine concentration

Juxta glomerular apparatus

- Area of contact between
  First part of DCT &
  Afferent & Efferent arterioles
- 3 types of cells :

① Juxtaglomerular cells Baroreceptors (Granular)
Epith like cells in media of Afferent arteriole.
Secrete Renin in response to :
a -- renal perfusion P
b -- NaCl conc. in macula densa (--GFR)
c β adrenergic stimulus

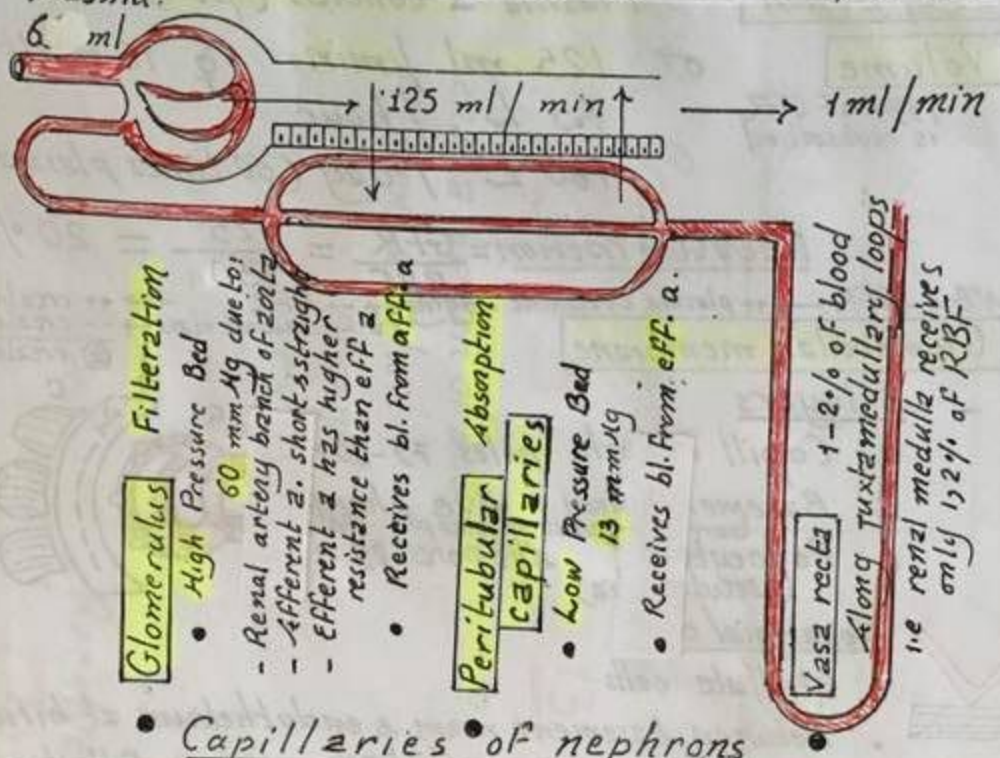
② Extraglomerular mesangial cells (Lacis cells)
Agranular cells at junction of Aff & Eff. arterioles
Location & function not known may store renin

③ Macula densa. Modified tubular cells
act as chemoreceptors which respond to changes in NaCl in DCT via tubuloglomerular feed back.
- If -- NaCl in DCT
  → ++ release of NO & PGs → VD of aff a
  → ++ renin → II → VC of Efferent a.
- If ++ NaCl in DCT
  → VC of afferent arteriole
  → -- GFR

- Function of JG app.
  Autoregulation of GFR & RBF
  of SAME nephron
  with changes in ABP
- Clinical significance
  Excess secretion of RENIN due
  e.g narrowing of renal artery
  tumour of juxtaglomerular cells
  → Secondary (renal) hypertension
  not responding to usual ltt of essential hypertension (medication & lifestyle)
  & Secondary hyperaldosteronism
  i.e ↑ Na^+ ↓ K^+ ↓ H^+ metabolic alkalosis

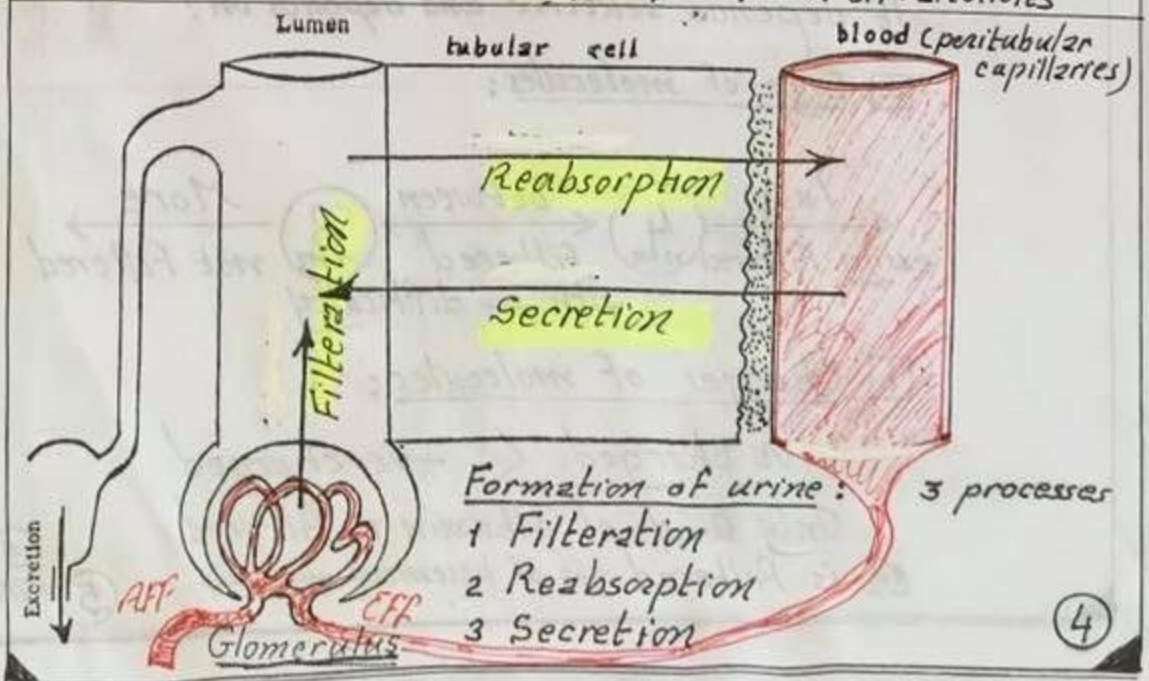
Renal blood Flow | RBF 20-25% of COP i.e 1.2-1.3 L/min

Renal artery → interlobar a → interlobular a → aff. arterioles → Glomerulus → eff. arteriole → peritubular capill. & vasa rectae



Autoregulation of RBF between ABP 90 - 220 mmHg

1. At high pressure: Intrinsic myogenic response.
   ++ ABP → stretch aff arteriole → ++ Ca^{++} influx → direct VC → ± RBF
2. At low pressure: a tubuloglomerular feedback. Discuss
   b Renin → ↑↑ → VC of eff. arterioles



Formation of urine: 3 processes

1 Filteration
2 Reabsorption
3 Secretion

Types of capillaries in nephrons:

Glomerulus	Peritubular Capill.	VASA RECTA
Filteration High Pressure bed. 60 mm Hg - Renal a. branch of aorta - Afferent a. short straight - Efferent a. Higher R than afferent a Receives blood from Afferent arteriole.	Absorption Low Pressure bed 13 mm Hg Receives blood from Efferent arteriole	Along juxtamedulla loop. Receives 1-2% of bl. i.e renal medulla receives only 1-2% of blood.

Glomerulus

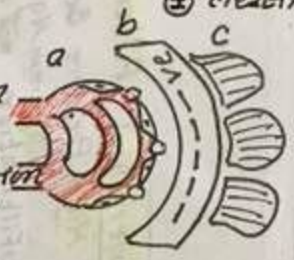
Glomerular filtrate is a ptn free ultrafiltrate 6 3 3

- **Composition** Plasma − colloids (ptn)
- **Volume** ♂ 125 ml / min. ♀ 10 % less
  (>99 % of GFR is reabsorbed) 7.5 L / hour
  180 L / day (60 times plasma vol.)

$$\text{Filtration fraction} = \frac{GFR}{RBF} = \frac{125}{6} = 20\ \%$$

N.B -- GFR → ++ plasma creatinine. Aging ↔ -- GFR → ++ creatinine; -- muscle mass → -- creatinine; ± creatinine

- **Glomerular membrane**
  - 3 layers
    - a Capill endoth. holes 79-90 nm
    - b Basement mem −ve charges barrier against plasma ptn filteration
    - c Podocytes (pseudopodia) slit pores 25 nm



  - Mesangial cells
    - Stellate cells
    - Between basement mem & endothelium at bifurcat.
    - Contractile cells —contract→ reduce filtrat. area
    - Takes up immune complex → glomerular diseases
  - Surface area 0.8 m^2
  - Permeability 50 times sk. ms capillary

It is highly selective and depends on:

[a] Size of molecules:

less ← (4 nm) easily filtered | between (8 nm) filtered with ++ difficulty | → More not filtered

[b] Charges of molecules:

−ve charged < +ve charged

Only 0.2 % of albumin is filtered

N.B loss of −ve charges of basement mem → albuminuria

Measurement of GFR

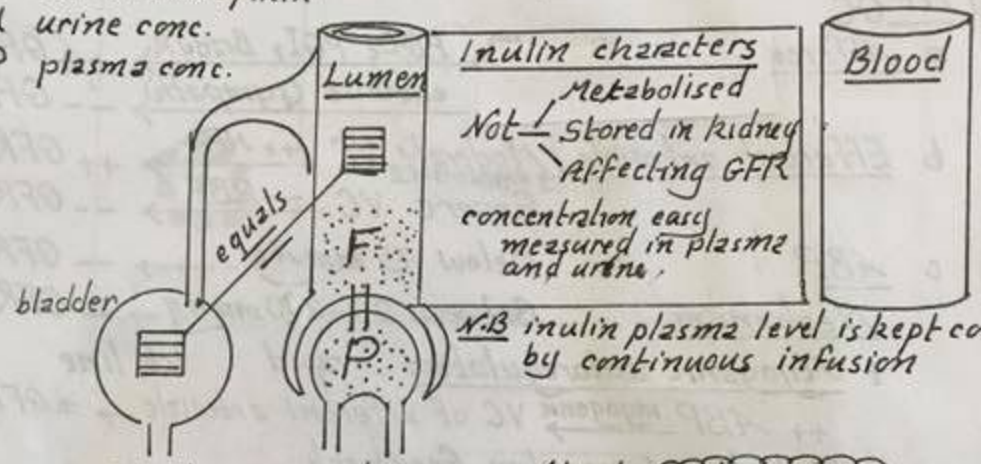
- Inulin clearance (found in dahlia tubers) Fructose MW 5200
  1. Freely filtered i.e plasma conc. = Filterate conc.
  2. Not reabsorbed or secreted

  So, Amount filtered = Amount excreted

  $GFR \times P(F) = V \times U$

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

V vol. of urine/min
U urine conc.
P plasma conc.



Inulin characters
Not Metabolised / Stored in kidney / Affecting GFR
concentration easy measured in plasma and urine.

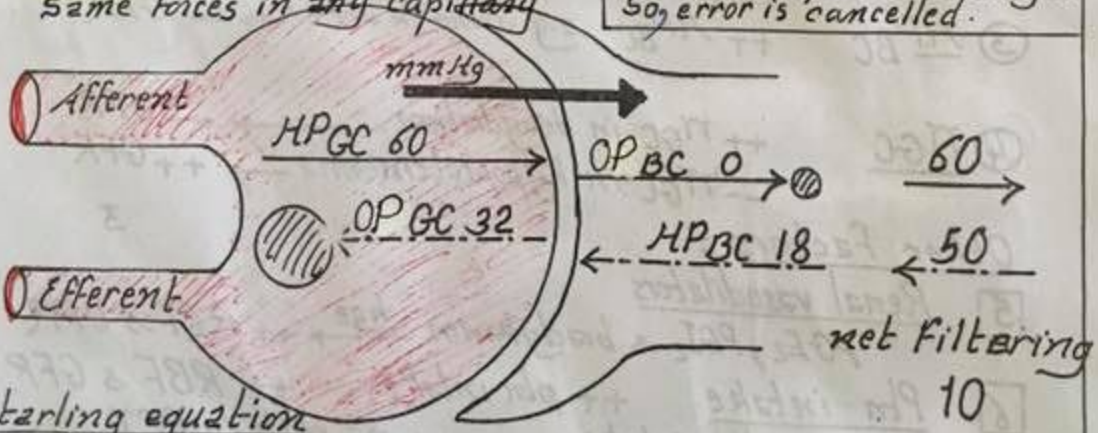
N.B inulin plasma level is kept constant by continuous infusion

- Creatinine clearance Advant: (endogenous) i.e no extra work is added to diseased kidney
- Radio isotopes as ^{51}Cr EDTA

Disadvant: Creatinine is partially secreted so, UxV is high
However, P also is high due to non specific chromogen
So, error is cancelled.

Forces that affect GFR

Same forces in ~~any~~ capillary



Starling equation

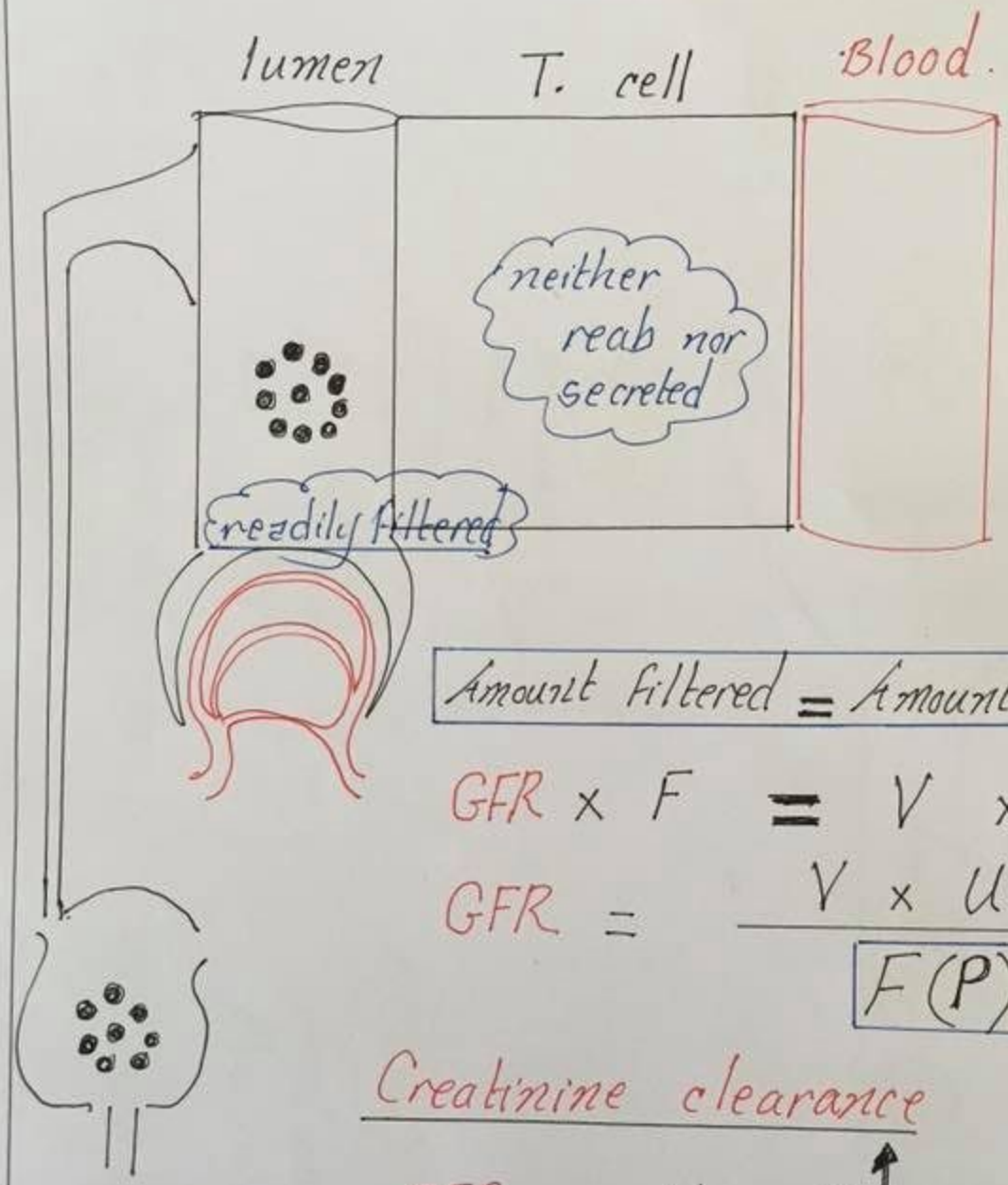
$GFR \propto (HP_{GC} + OP_{BC}) - (HP_{BC} + OP_{GC})$

$= K_F$ net filtering pressure

K_F depend on [area, Permeability] Glom. membrane

Measurement of GFR

Inulin clearance



Amount filtered = Amount excreted

$$GFR \times F = V \times U$$

$$GFR = \frac{V \times U}{F(P)}$$

Creatinine clearance

$$GFR = \frac{V \times U \uparrow}{P \uparrow}$$

Factors that affect GFR 4 + 2

Factors involved in Starling equation: 4

① K_F ++ K_F ⟶ ++ GFR

a permeability: ++ thickness ⟶ -- K_F (uncontrolled DM, hypertension)

b surface area:

1 Contraction of mesangial cells ⟶ -- area

2 Relaxation of " " ⟶ ++ area

3 Uncontrolled DM (-- glom. capill) ⟶ -- area

② HP_{GC}

a Afferent arteriole VD (PGE2, PGI_2, Bradyk.) ⟶ ++ GFR

VC (exercise (sympath)) ⟶ -- GFR 50%

b Efferent arteriole Moderate VC (e.g. angiotensin II) ⟶ ++ HP_{GC} ⟶ ++ GFR

Severe VC ⟶ -- RBF ⟶ -- GFR

c ABP Below 75 mmHg ⟶ -- GFR

Mechanism Between 90–220 mmHg ⟶ ± GFR

1 Myogenic autoregulation rapid 1st line

++ ABP ⟶ myogenic VC of afferent arteriole ⟶ ± GFR

2 Tubulo-glomerular feedback

++ ABP ⟶ ++ RBF & GFR ⟶ ++ NaCl at macula densa

secrete ⟶ adenosine ⟶ VC of afferent arterioles

⟶ -- RBF & GFR to normal & vice versa

-- ABP ⟶ -- RBF & GFR ⟶ -- NaCl reab in ascending limb of loop ⟶ -- NaCl at macula densa which sends signals ⟶ VD of aff and VC of eff. arterioles viz renin

③ HP_{BC} ++ HP_{BC} e.g. stone in ureter ⟶ -- GFR

④ OP_{GC} ++ GC in dehydration ⟶ -- GFR

-- GC in hypoproteinemia ⟶ ++ GFR

Other Factors: 3

⑤ Renal vasodilators

PGE_2, PGI_2 & bradykinin ⟶ hge ⟶ ++ RBF & GFR

Aspirin ⟶ -- PGs ⟶ -- RBF & GFR

⑥ Pln intake ++ pln intake ++ RBF & GFR

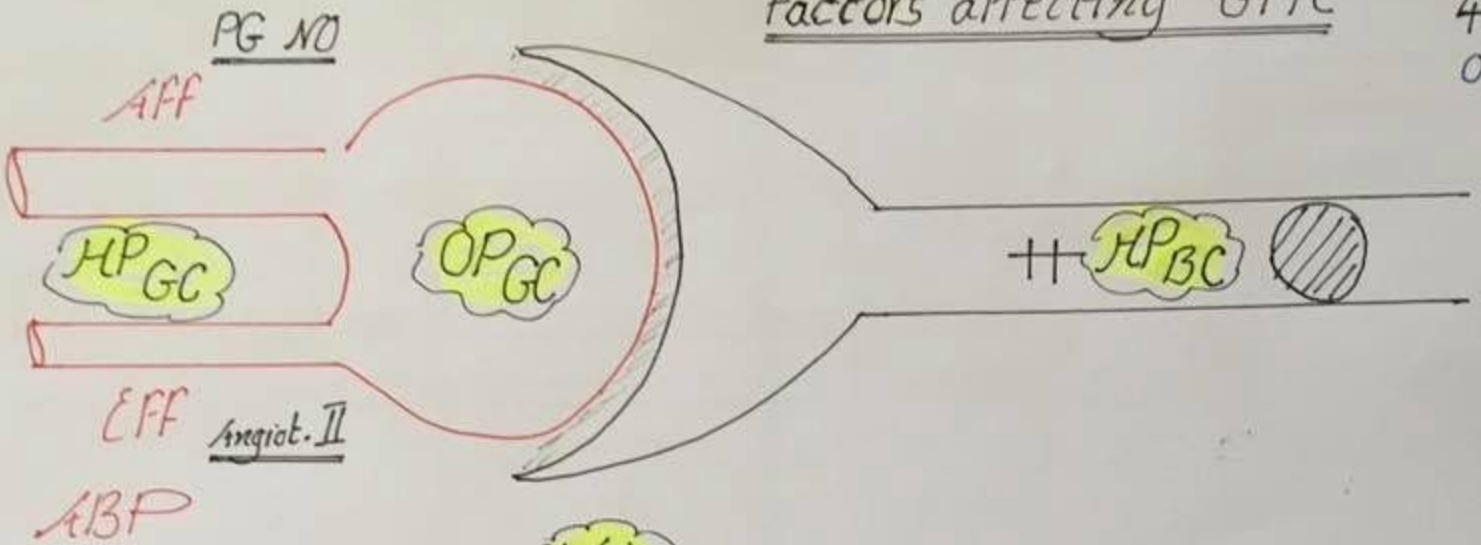
++ pln intake ⟶ ++ aa reab in PCT ⟶

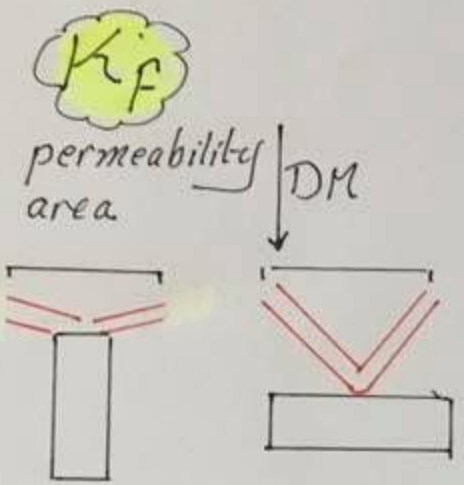
++ NaCl reab ⟶ -- NaCl at macula densa ⟶

VD of afferent and VC of efferent ⑦

Factors affecting GFR

4 Forces other





Others

renal vasodilator
Ptn intake.

5 Other factors — Renal vasodilators, Ptn intake — PGs ≠ Aspirin

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