Excretory system

Endocrine functions of kidney

Hormones secreted by kidney are:

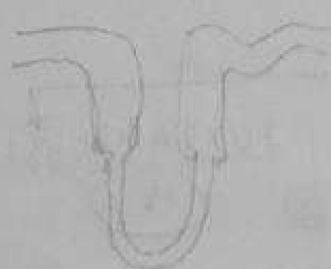
(i) Erythropoitein - RBC product
(ii) Thrombopoietin
(iii) Renin - ↑BP
(iv) Calcitriol (1,25-dihydroxy chole calciferol) - Vit D
25-hydroxycholecalciferol
1α-hydroxylase
(v) Prostaglandins - inflammation

Types of Nephrons

CORTICAL or superficial NEPHRONS	JUXTAMEDULLARY NEPHRONS
(i) 85%	(i) 15%
(ii) Renal corpuscles in outer cortex near periphery.	(ii) Renal corpuscle in inner cortex near medulla.
(iii) Loop of Henle - short; dips very little ~~ont~~ into the medulla.	(iii) LOH - long; dips deeps into the medulla upto the tip of papilla.
(iv) Blood supply - peritubular capillaries	(iv) Vasa Recta.
(v) Function - Urine formation	(v) mainly urine concentration & also urine formation.

LOOP OF HENLE: flattened epithelium

- Descending limb
  - Thick descending segment
  - Thin descending segment
- Hairpin bend
- Ascending limb
  - Thin ascending segment
  - Thick ascending segment



JUXTAGLOMERULAR APPARATUS

→ Juxtaglomerular apparatus is a specialized organ situated near the glomerulus of each nephron.

* **Structure of JGA:** JGA is formed by 3 different structures:-

(i) Macula densa.
ii> Extraglomerular mesangial cells./Lacis cells
iii> Juxtaglomerular cells./granular cells.

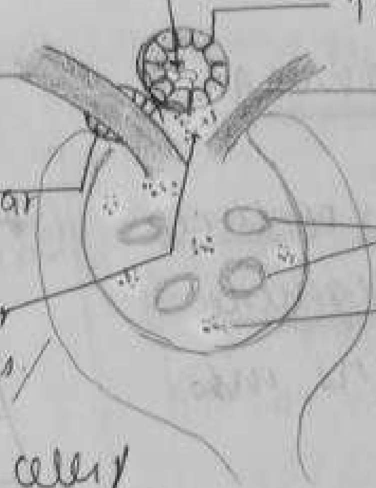

(i) Macula densa
Thick ascending ligment
Afferent Arteriole
Efferent Arteriole
(iii) juxtaglomerular cells.
capillaries
(ii) Extraglomerular mesangial cells.
Lacis cell
Agranular cells/
goormaghtigh cells.
Glomerular mesangial cells/
~~Granular cells~~.

Fig: JGA.

MACULA DENSA

(i) end portion of thick ascending segment of Lyn before it opens into DCT.

(ii). int b/w afferent & efferent arteriole of same nephron.

(iii). very close to afferent arteriole.

(iv). formed by tightly packed cuboidal epithelial cells.

(v). sensitive to NaCl in tubular fluid.

LACIS CELLS / AGRANULAR CELLS / GOORMAGHTIGH CELLS EXTRAGLOMERULAR MESANGIAL CELLS.

(i) int in angular region bounded by
Afferent Arteriole
Efferent "
Macula densa

(ii) secrete PG

INTRAGL... MESANG...
GLOMER... MESAN...

(i) another mesan... b/w capil... glom... ce...

(ii) ... ca... ... ro... o...

(iii)

INTRAGLOMERULAR MESANGIAL CELLS / GLOMERULAR MESANGIAL CELLS

(i) another type of mesangial cells present in b/w glomerular capillaries called glomerular mesangial cells.

(ii) support glomerular capillary loops by surrounding the capillaries in the form of cellular network.

(iii) Function :-

① regulate glomerular filtration by contractile property.

② phagocytic

③ secrete – glomerular interstitial matrix
– PGs
– cytokines.

GRANULAR CELLS / JUXTA GLOMERULAR CELLS

(i) ~~are~~ specialised smooth muscle cells

(ii) present in the wall of afferent arteriole just before it enters the Bowman's capsule.

(iii) These smooth muscle cells are mostly present in tunica media & tunica adventitia on the wall of afferent arteriole.

(iv) called granular cell ∵ presence of secretory granules in their cytoplasm
→ renin

FUNCTIONS OF JGA.

(I) 1° function - hormone secretion.

(i) regulates [glomerular blood flow & GFR.

(I) HORMONE SECRETION.

→ JGA secretes 2 hormones
(i) Renin - by JG cells/granular cells
(ii) PG. - secreted by Lacis cell/ extraglomerular mesangial cells of JGA.

• also secreted by interstitial cells of Medulla called Type I Medullary interstitial cells.

RENIN.

(i) ↓ arterial bp.
(ii) ↓ ECF vol.
(iii) sympathetic stimul...
(iv) ↓ plasma Na+ & Cl-
Re...

Angiotensin...
me in [RBCs
vascu...
Medu...

RENIN.

plasma.

(i) ↓ arterial bp.
(ii) ↓ ECF vol.
(iii) sympathetic stimulation
(iv) ↓ plasma Na+ & Cl-

⊕ Renin →

Angiotensinogen
↓
Angiotensin I
(decapeptide)

ACE (lungs) →
↓

★ most active
Angiotensin II
(Octapeptide) →

Angiotensinases → mt in [RBCs, vascular beds.
↓
Angiotensin III
(heptapeptide) → [↑se aldosterone secretion, vasoconstriction.
↓
Angiotensin IV
(hexapeptide)

LONG TERM ARTERIAL B.P.

AUTOREGULATION OF B.P. BY KIDNEY OR

REGULATORY MECHAN[illegible]

DIRECT MECHANISM

RENAL FLUID MECHANISM / ECF VOLUME " mechanism

INDIRECT [illegible]

⊖

→ Blood loss / ↓ B.P. (H[illegible]

[illegible]emorrhage / Dehydration)

RENAL ISCHEMIA (blood to kidney ↓)

↓ Afferent Arteriole P

↓ NaCl delivery to MACULA DENSA

↓⊕ BAROR[illegible]

↓⊖ ↑ symp[illegible]

has the quality to the blood vol

JG Cells (kidney) Release $\boxed{\text{Renin}}$

⊕

Angiotensinogen (Liver)

Medium — (CAPOTEN) — CAPTOPRIL — ~~(A-ACTRO)~~ inhibit

⊖

Lungs on vascular epithelium → ACE

Angiotensin I

Angiotensin II

on blood vessels

VASOCONSTRICTOR

↓

↑se sympathetic tone

↓

↑se Noradrenaline

ALDOSTERONE (of Adrenal cortex) — Zona Glomerulosa

- Na^+ & H_2O reabsorption ↑
- K⊕ excretion ↑
- maintain electrolyte balance

ADH → ↑se the absorption of H_2O

→ ↓ses H_2O loss through urine

↑se blood vol.

↓

B.P. ↑

⊖

FUNCTIONS OF ANGIOTENSIN-II

On Kidney

① Regulates GFR in 2 ways:

constrict efferent arteriole ⇓ (vasoconstriction)

contract glomerular mesangial cells ↓ ↓ in S.A of glomerular capillaries & filtration

On brain

BARORECEPTOR REFLEX ⇓ B.P ↑

↑ses H₂O uptake stimulates thirst centre

Hypothalamus → Corticotropin Releasing Hormone ↑ (CRH), ADH ↑

PITUITARY ↓ ↑ ACTH

07/05/19.

FILTRATION FRACTION

- fraction/ portion of renal plasma, which leaves the filtrate.
- It is the ratio of GFR & renal plasma flow.
- It is expressed in %.

$$\boxed{F.F = \frac{GFR}{\text{Renal plasma flow}} \times 100\%}$$

$$= \frac{125 \text{ ml/min}}{650 \text{ ml/min}} \times 100$$

$$= 19.2\%$$

- Normal filtration fraction ⇒ 15-20%.

FACTORS AFFECTING (REGULATING) GFR:-

1) **RENAL BLOOD FLOW** most imp. factor.

$\boxed{\text{GFR} \propto \text{renal blood flow}}$

Normal blood flow to kidney - 1300 ml/min.

Regulation of Renal blood flow

* **AUTOREGULATION:**

• intrinsic ability of an organ to regulate its blood flow.

• Autoregulation is nt in some vital organs - heart, brain, kidney.

i) **Renal autoregulation**:- imp to maintain GFR.

→ Renal blood flow ~~remains~~ remains normal even when the mean arterial b.p. vary b/w 60-180 mmHg.

② **Mechanisms of autoregulation**

① **Myogenic Response**:-

blood flow to kidney ↑

⇓

elastic wall of afferent arteriole is stretched

⇓

influx of Ca^{++} from ECF into cells

⇓

contraction of smooth m/s of afferent arteriole

⇓

constriction of afferent arteriole

⇓

↓ blood flow.

② Tubuloglomerular feedback:
· mechanism to regulate GFR through renal tubule & macula densa.
└ of JGA is sensitive to NaCl in tubular fluid

↑ GFR
⇓
↑[NaCl] in renal tubule
⇓
Macula densa release
↓
adenosine from ATP
↓ via adenosine A₁ receptor
constriction of afferent arteriole
↓
↓ glomerular blood flow
→ Tubuloglomerular feedback → ↓ GFR

Sensitivity of Tubuloglomerular feedback

↑sed
(i) Adenosine - vasoconstrictor
(ii) Thromboxane
(iii) PGE_2 - vasodilator

↓sed
(i) cAMP
(ii) cAMP.
(iii) $PG\text{-}I_2$
(iv) nitrous oxide

Tubulo-glomerular feedback

$\boxed{GFR \downarrow}$

↓

↓ [NaCl] in renal tubules

↓

Macula densa release.

$\boxed{PG-E_2}$	$\boxed{Bradykinin}$	$\boxed{Renin}$

PG-E2, Bradykinin → dilation of afferent arteriole.

Renin ↓ ⊕ Angiotensin II ↓ constriction of efferent arteriole.

↓

↑ GFR & glomerular blood flow

---

③ ↑ Glomerular capillary P :- ∝ GFR ↑

④ colloidal osmotic P : ↑ ∝ $\frac{1}{GFR \downarrow}$ (25 mmHg)

↓

exerted by plasma pr. in glomerular capillary blood

⑤ Hydrostatic P in bowman's capsule ↑ ∝ $\frac{1}{GFR \downarrow}$

⑥ constriction of afferent arteriole :→ ↓ blood flow ↓ ↓ GFR.

⑦ constriction of efferent arteriole → ↑ GFR.

Regulation of Tubular Reabsorption

1) Glomerulotubular Balance
↓
balance b/w filtration & reabsorption of water & solutes in kidney.

process helps in constant reabsorption of Na & H_2O from renal tubules

GFR ↑
↓
tubular load of solutes in PCT & water in PCT ↑
↓
↑ reabsorption of solutes & water
↓

Mechanism of glomerulotubular balance

occurs ∵ of osmotic P in peritubular capillaries

GFR ↑
↓
↑ amt of plasma pr accumulate in peritubular capillaries & blood
↓
↑ osmotic P in peritubular capillaries
↓
↑ reabsorption of Na+ & H_2O from tubules into capillary blood
↓
GFR ↓

Reabsorption of important substances.

1) Reabsorption of Na+ :-

From the glomerular filtrate, 99% of Na+ is reabsorbed.

- 2/3rd of Na+ is reabsorbed in PCT.
- Remaining (1/3rd) - Reabsorbed in other segments (except descending limb) & collecting duct

* Na+ Reabsorption occurs in 3 steps:-

1) Transport from the lumen of Renal tubules into tubular epithelial cells:-

Active transport — occurs in 2 ways.

i) $\boxed{\text{Antiport}}$ - in exchange for H+ in PCT.
 └ Na+ counterport pr.

Na+ H+

ii) $\boxed{\text{Symport}}$ - Na+ cotransport pr along with other subs. like AA & glucose
 └ in other segments & collecting duct.

AA/Glu
Na+

- some amt of Na+ diffuses from lumen into tubular epithelial cells a/c to electrochemical gradient.
  ↓
  developed by Na-K pump.

(ii) Transport from tubular epithelial cells into interstitial fluid:-

by Na^+-K^+ pump.

$2K^+ \leftarrow$ ATP $\rightarrow 3Na^+$, ADP

tubular cell. interstitial fluid

↓[Na^+] inside cell → electrochemical gradient b/w cell & ECF.
↓
diffusion.

(iii) Transport from interstitial fluid into blood:
→ by conc. gradient.

* In DCT - reabsorption of Na^+ & H_2O
↑ ⊕
aldosterone ← adrenal cortex.
↓ ⊕
excretion of K^+

(II) REABSORPTION OF WATER
from PCT, DCT & collecting duct

(i) Reabsorption of water from PCT - Obligatory H_2O Reabsorp
• Reabsorption of H_2O from PCT is secondary (obligatory to Na^+).

Na+ reabsorbed from PCT
⇓
O.P ↓
⇓
osmosis of H_2O from renal tubules

(ii) Reabsorption of water from DCT & collecting duct: Facultative water Reabsorption:-
occurs by the activity of ADH

• Normally, DCT & C.T - impermeable to H_2O.

$\xrightarrow[\text{Vasopressin}]{\text{ADH}}$ permeable to H_2O.

ADH combines with vasopressin (V_2) receptors in tubular epithelial membrane

↓ ⊕

$\boxed{A.C}$ Adenyl cyclase

↓ ⊕

ATP ⟶ cAMP

↓ ⊕

AQP - membrane pr
function as H_2O channels.

↓

↑ H_2O reabsorption

(iii) Reabsorption of glucose:-

* Glucose - completely reabsorbed by PCT
  └ transported by 2° active transport
    ↓
    Na cotransport mechanism

(a) * Na+ + Glucose —(SGLT-2)→ enter the cell
Na+-dependent glucose cotransporter-2.

Binds to common carrier pr. in luminal membrane of tubular epithelium

(b) Glucose
Tubular cell —(GLUT-2)→ medullary interstitium
Glucose transporter-2.

* Tubular max. for glucose (Tmg):-
Adults [♂ - 375 mg/min
♀ - 300 mg/min

* Renal threshold for glucose:-
180 mg/dl in venous blood

* when blood level reaches 180 mg/dl
↓
Glucose ‡ completely reabsorbed
↓
appears in urine → GLYCOSURIA

CONCENTRATION OF URINE

When water content in the body ↑ses, kidney retains H_2O & excretes conc. urine

* (2) processes:-

1) Development & maintainance of medullary gradient by countercurrent mechanism.

2) Secretion of (ADH) - facultative H_2O reabsorption
H_2O impermeable [DCT, CT] → permeable to H_2O

(1) Medullary Gradient

→ Cortical interstitial fluid is isotonic to plasma with osmolarity (300 mOsm/L)

→ osmolarity ↑se gradually from outer part towards inner medulla.

→ Osmolarity is max. at the innermost part of medulla near renal sinus. It is hypertonic with osmolarity of (1200) mOsmol/L.

→ This type of ↑se in osmolarity of medullary interstitial fluid is called medullary gradient.
↓
imp. role - conc.^n of urine

Isotonic to plas…
300mOsm/L
cortex
outer medu…
inner med…
1200
hypert…
→ Develop…
Count…
* Coun…
is a
flow
tubu…
→ Div…

COUNTER CURRENT MULTIPLIER

→ LOOP OF HENLE : functional
responsible for — hyperosmolarity of medullary interstitial fluid
— medullary gradient

→ Role of Loop of Henle in development of juxtamedullary nephrons :—
functions as countercurrent multiplier ∵ loop of these nephrons is long & runs deep into the medulla.

→ Main reason for hyperosmolarity of medullary interstitium:—

active reabsorption of NaCl & other solutes from ascending limb of loop of Henle into medullary interstitium

⇓

solutes accumulate in medullary interstitium

↓

↑se the osmolarity

→ Now due to conc. gradient

↓

Na^+ & Cl^- diffuse from medullary interstitium into the descending limb of LofH.

↓

reach ascending limb via hairpin bend.

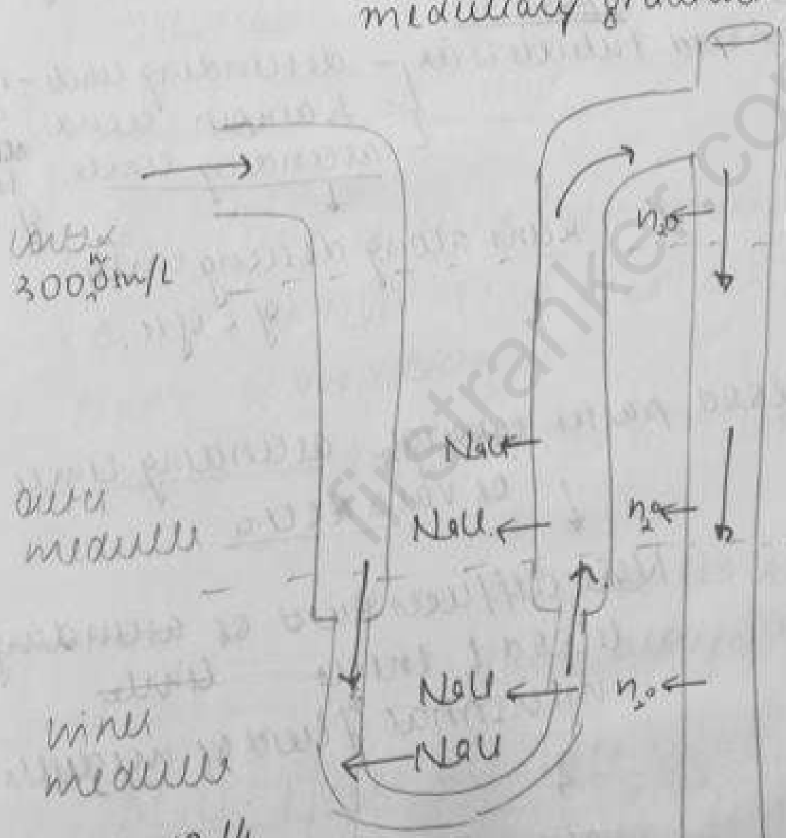
→ Na^+ & Cl^- - repeatedly recirculated b/w ascending limb & descending limb through medullary interstitial fluid leaving small portion to be excreted into urine

⇒ Apart from this, there is regular addition of Na^+ & Cl^- into descending limb by constant filtration

∴ Reabsorption of NaCl from ascending limb &
addition of new NaCl ions into descending limb

↓

Inc / multiply the osmolarity of medullary interstitial fluid & medullary gradient.



Other factors responsible for hyperosmolarity of medull. inter. fluid

(i) Reabsorption of Na^+ from collecting duct

(ii) Recirculation of urea.

COUNTERCURRENT EXCHANGER

- Vasa recta function as ↑
- It is responsible for maintainance of medullary gradient which is developed by countercurrent multiplier.

→ Role of Vasa Recta in the maintainance of NaCl grad

↓

acts like counter current exchanger because of its *position.

- It is 'U' shaped tubule with – descending limb – runs along asc limb of LoH
  - hairpin bend
  - ascending limb ↓ runs along descing limb of LoH.

→ When blood passes through ascending limb of vasa Recta

↓

NaCl diffuses out of ~~ascending~~ blood & enters ~~limb~~ interstitial fluid of medulla

&

water diffuses into blood

∴ Vasa Recta retains NaCl in medullary interstitium & removes H_2O from it

∴ Hyperosmolality is maintained

Cortex

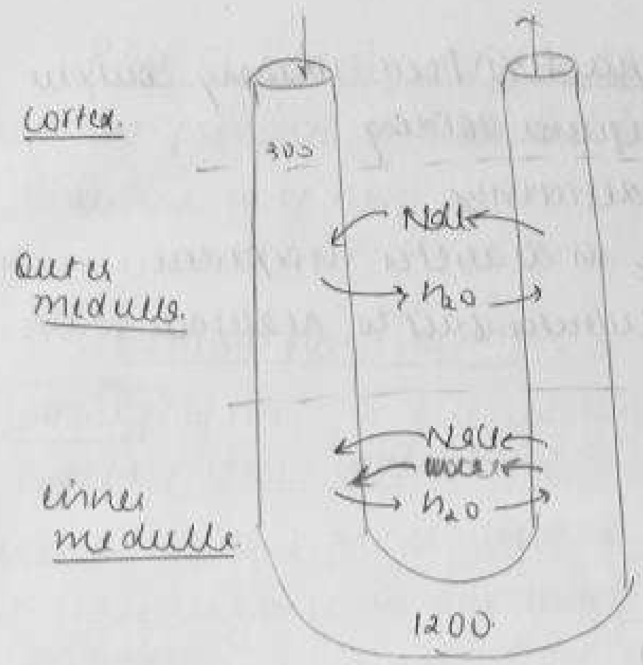
Outer medulla

inner medulla

* Recycling
- along with limb of

∴ NaCl ascen

∴ H₂O



* Recycling of urea also occurs through vasa recta
. along with NaCl, some urea also enters descending limb of vasa recta

Blood passes to ascending limb of vasa recta.
↓
urea diffuses back to medullary interstitium alongwith NaCl.

∴ NaCl & urea are exchanged for water b/w ascending & descending limb of vasa recta.
∴ This system is called countercurrent exchanger

+ polyuria: (1) ↑sed urinary output with frequent voiding.

(2). ADH deficiency.

(3). common in diabetes incipidus.

4. renal tubules fail to reabsorb water.

Role of Kidney in acid-Base Balance

→ Kidney prevents metabolic acidosis by ② ways:-
i) Reabsorption of HCO_3^-
ii) secretion of H^+.

i) Reabsorption of HCO_3^-

① ~4320 meq of HCO_3^- is filtered everyday by the glomeruli
② It is called filtered load of HCO_3^-.
③ Excretion of this much HCO_3^- in urine will affect acid-base balance in our body.
④ So, HCO_3^- must be taken from renal tubules by reabsorption.

ii) Secretion of H^+

① Reabsorption of filtered HCO_3^- occurs by the ~~reabsorption~~ secretion of H^+ by renal tubules.

② ~4380 meq of H^+ appears everyday in renal tubules by [filtration, secretion.

↓

most of them is utilised for HCO_3^- reabsorption.

③ → Only 50-100 meq is excreted] results in acidification of urine.

④ * secretion of H^+ into renal tubules occurs by the H_2O release form of H_2CO_3
→ into PCT, DCT & CD
→ by ② pumps [Na^+-H^+ antiport pump, proton pump.

Removal of H^+ & Acidification of Urine

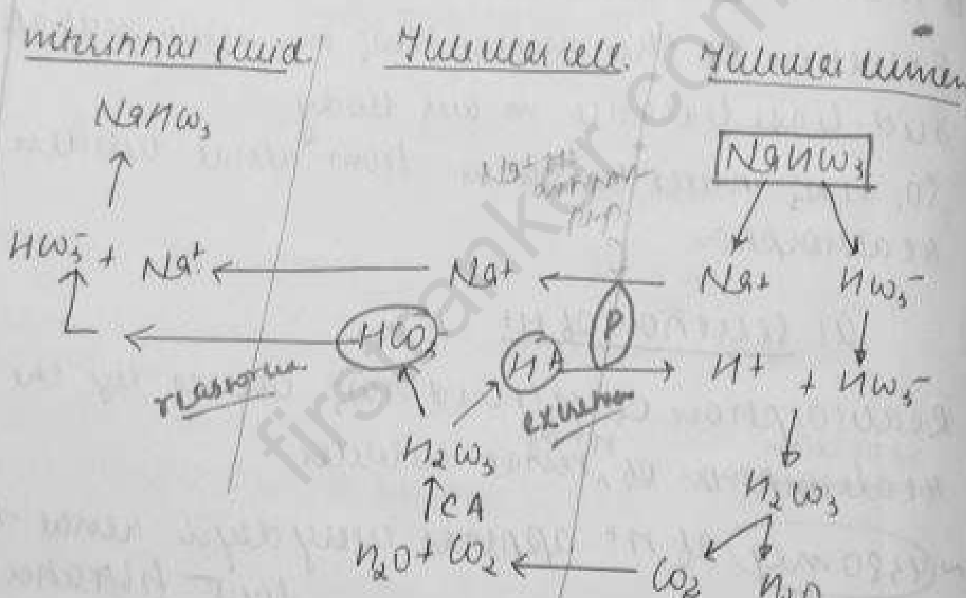
by 3 mechanisms:-

i) HCO_3^- mechanism

ii) NH_3 mechanism

iii) PO_4^{-3} mechanism.

i) Bicarbonate Mechanism:- mainly (PCT)



- For every H^+ secreted into lumen of tubule, 1 HCO_3^- is reabsorbed from tubule.
- In this way kidney conserve HCO_3^-.
- Reabsorption of HCO_3^- - imp factor for maintaining pH of body fluids.

ii) PO_4^{-3} Mechan

Interstitial flu

$NaHCO_3$

Na^+

HCO_3^-

reabs

Excre

iii) Ammonia

Interstitial Flu

Na^+

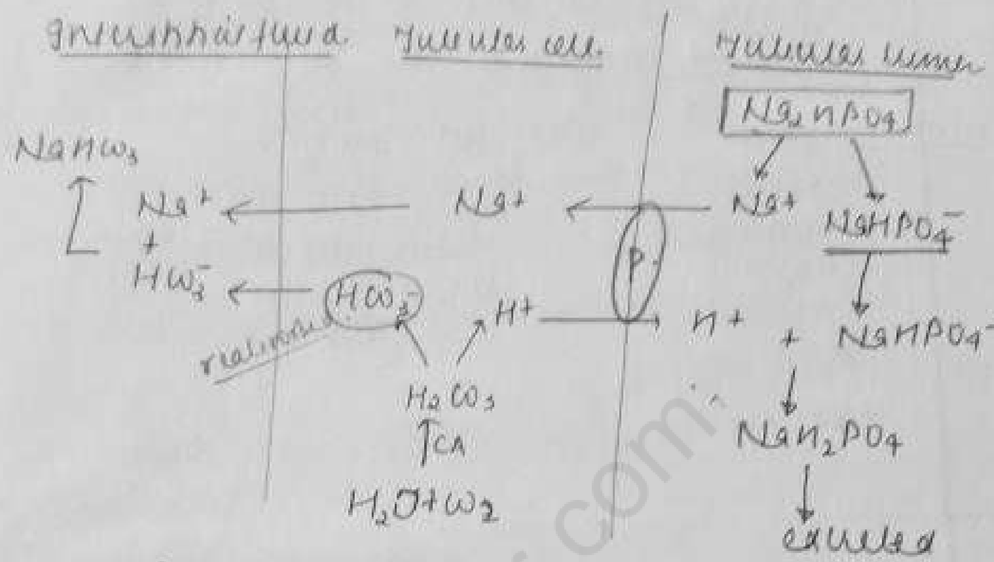
$Na^+ + HCO_3^-$

$NaHCO_3$

∴ By cons

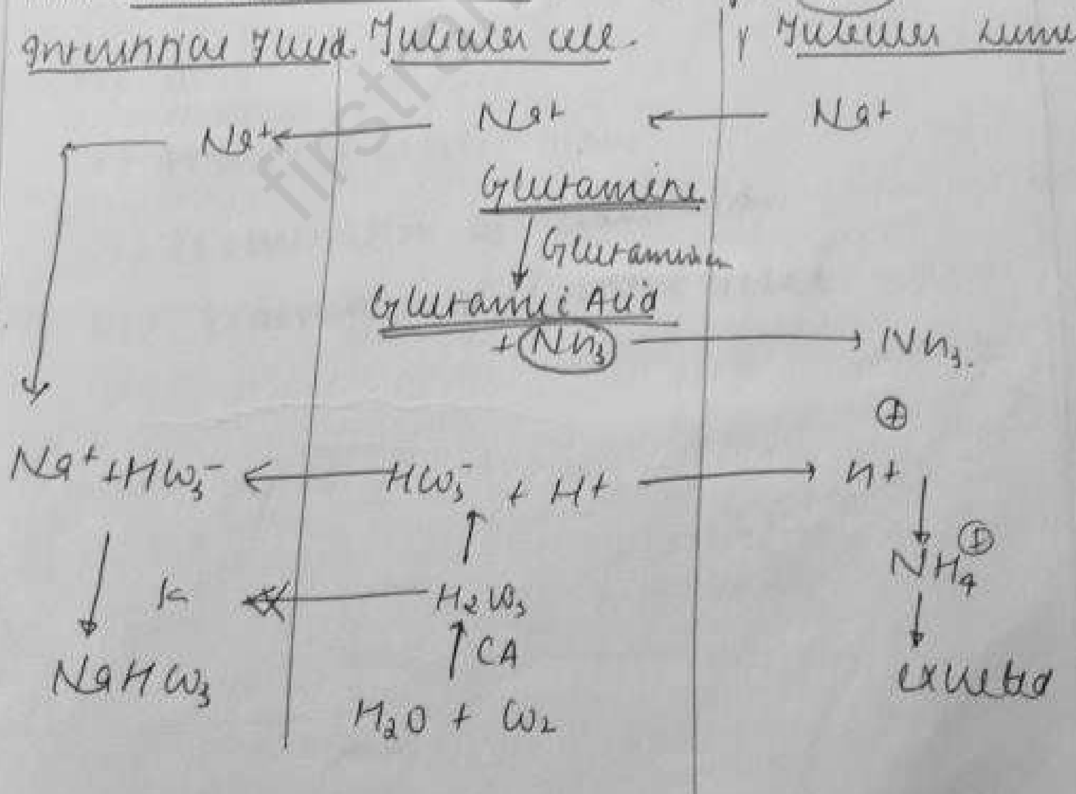
acidic ur

ii) PO_4^{-2} Mechanism :- mainly in (DCT) & (CD)



⟶ Excretion of H+ in combination with phosphate ion

iii) Ammonia mechanism :- mostly in (PCT)



∴ By conserving HCO_3^- & excreting H+, kidneys produce acidic urine & helps to maintain pH balance of body fluid

Composition of Urine (pn-45-6)

- Water
- Solids
  - Organic substance
    - i) urea
    - ii) uric Acid
    - iii) creatinine
    - (v) NH_3
  - Inorganic salts
    - i) Na^+
    - ii) K^+
    - iii) Ca^{++}
    - iv) Cl^-
    - v) PO_4^{-3}
    - vi) SO_4^{-2}

Biochemistry

Renal Function Tests:-

group of tests that are performed to assess the function of kidney.

③ types:-

i) Examⁿ of urine alone.

ii) Examination of blood alone.

iii) Examination of urine & blood

10/05/19

EXAMINATION of Urine - Urinalysis

→ Routine examination of urine/urinalysis is a gap of diagnostic test performed on the sample of urine.

→ Urinalysis is done by :-

i> physical examination - vol, color, appearance
ii> microscopic examination.
iii> chemical analysis. - to analyse abnormal constituents in urine like (i) Glucose, (ii) pr, (iii) Bile salt, (iv) Blood, (v) Ketone bodies

EXAMINATION OF BLOOD & URINE.

① **Measurement of GFR:-** A substance that is completely filtered but neither reabsorbed nor secreted should be used to measure GFR.

⇒ **Inuline** - ideal substance used to measure GFR
- neither reabsorbed nor secreted
- completely filtered

∴ Inuline indicates GFR

(i) **Inulin Clearance:-**

+ Proced → known amount of Inulin injected into body

⇓

After sometime

⇓

[Inulin] in plasma / urine & vol of urine excreted — estimated

Ex:- [Inulin] in urine = 125 mg/dL.
 " " plasma = 1mg/dL.
 vol. of urine output = 1ml/min.

$$\therefore GFR = \frac{125 \times 1}{1} = \boxed{125\ ml/min}$$

① Creatinine Clearance :- used to measure GFR
└ easier than inulin clearance

∵ creatinine is already present in the body fluids
&
its plasma concentration is steady throughout the day

→ Creatinine is completely filtered &
being a metabolite, it is neither secreted nor reabsorbed

- The normal value of GFR determined by creatinine clearance ≃ value of GFR determined by inulin clearance

② MEAS

→ To me

② MEASUREMENT OF RENAL PLASMA FLOW

→ To measure renal plasma flow.
a substance which is filtered & secreted ≠ reabsorbed should be used

- Ex- p. NH_2 hippuric acid (PAH)
- PAH clearance indicates the amt. of plasma passes through kidney
- A known vol. of PAH - injected into body
↓
PAH is concentrated
↓
*[PAH] in urine, plasma
*vol of urine excreted
estimated

Renal plasma flow = $\frac{[PAH]urine \times vol\ of\ urine\ output}{[PAH]plasma}$

= 660 ml/min

⇒ UREA CLEARANCE TEST

↓ Clinical test to assess the clearance of urea from plasma by kidney every min.

→ Test requires:-

i) blood sample to determine urea level in blood.

ii) ② urine samples collected at 1 hr interval to determine the urea cleared by kidney into urine.

- Normal value of urea clearance = 70ml/min

→ Urea:-

- waste pr- formed during pr. metabolism
- excreted into urine

Determination of urea clearance forms a specific test to assess kidney / renal function.