

INTEGRATED RENAL SYSTEM

RENAL PHYSIOLOGY

Clearance = $\frac{U_x \times V}{P_x}$ (ml/min)
 GFR = C_{inulin}
 RPF = C_{PAH}
 Filtration fraction = $\frac{\text{GFR}}{\text{RPF}} \approx 20\%$
 $\text{RBF} = \frac{\text{RPF}}{1 - \text{Hct}}$
 Clearance: **PAH** > **Creatinine** > **Inulin** > Urea > Na > Glucose

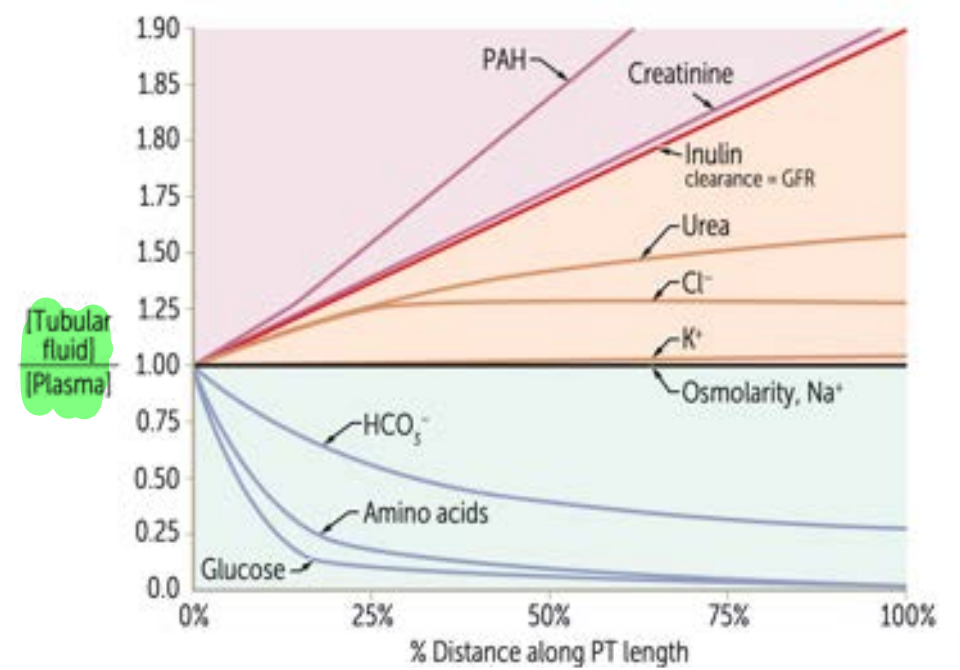
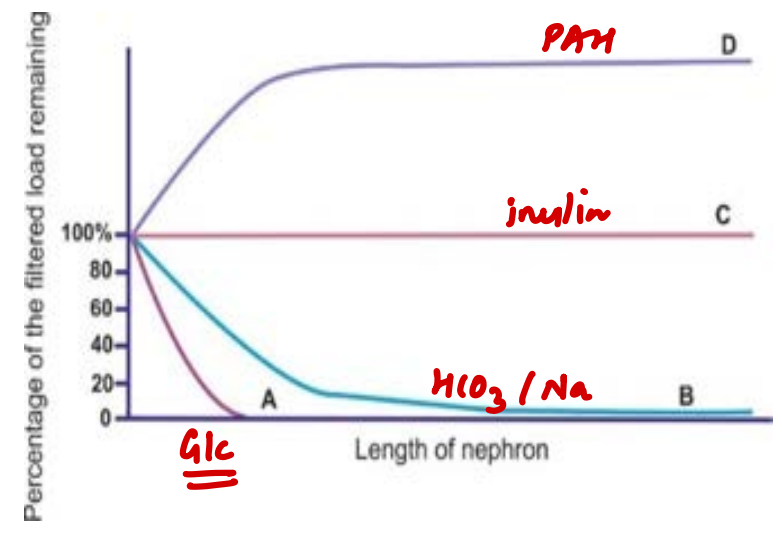
Counter-current:
 CC multiplier = **MAIN** LOH
 CC exchanger: *Vasa recta*

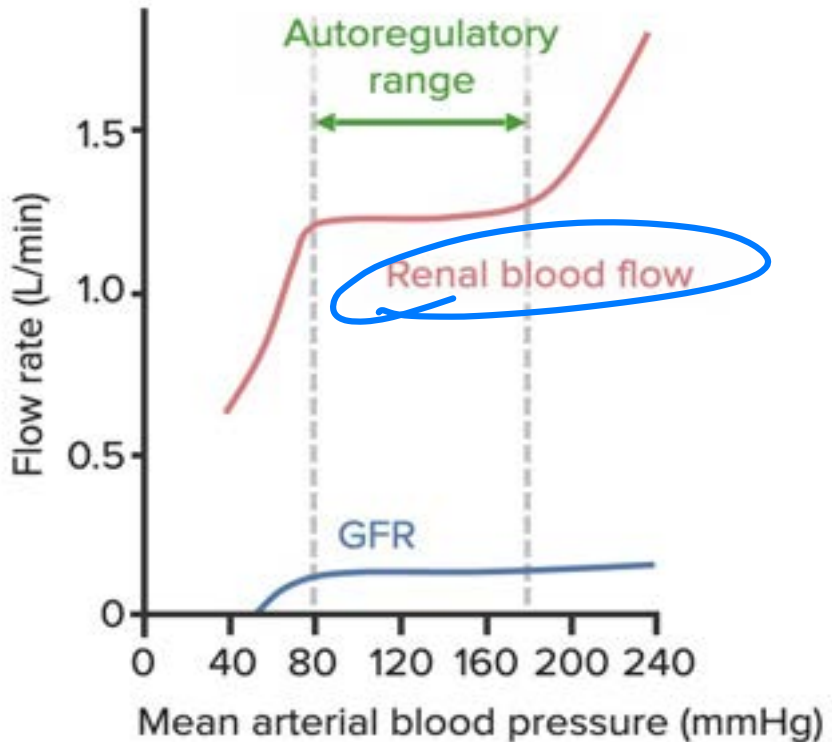
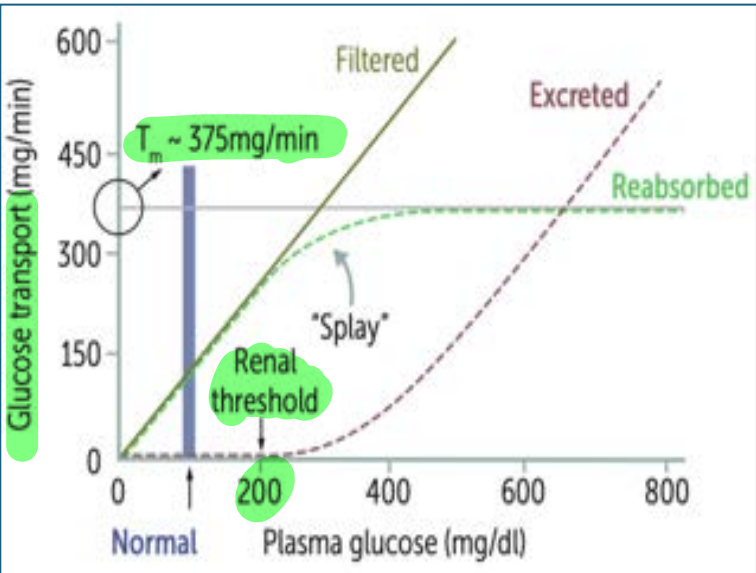
Macula Densa

- chemosensor
- DCT - TAL
- Tubulo-glomerular feedback
- $\uparrow \text{Na}^+$ → adenosine → aff arteriole VC → **GFR ↓**

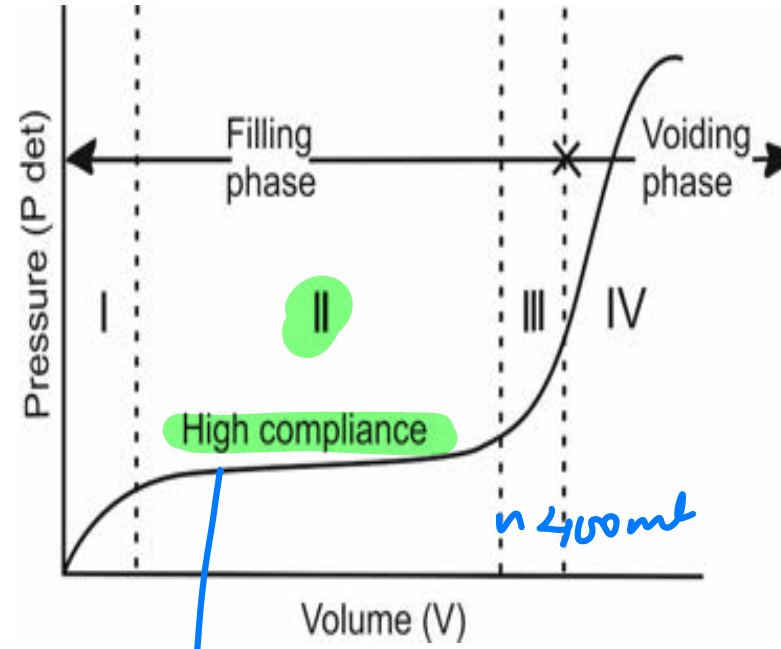
Juxtaglomerular cells

mod smooth muscle cells afferent arteriole
 $\downarrow \text{BP} \rightarrow \text{RAAS}$ (Renin → Angiotensin → **ALDOSTERONE**)
 $\uparrow \text{B}_1$ (sym stim)



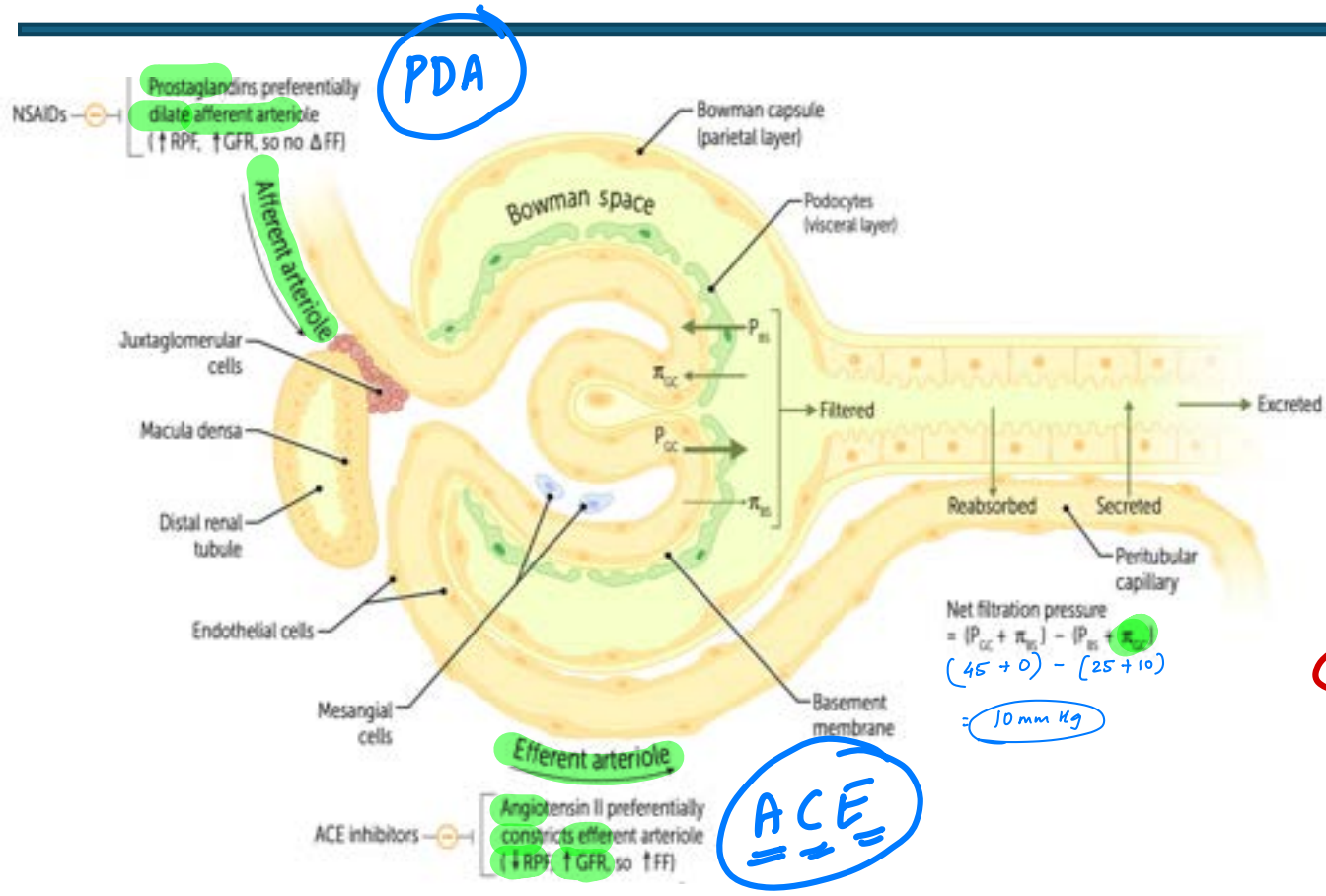


80 - 200 mm Hg MAP



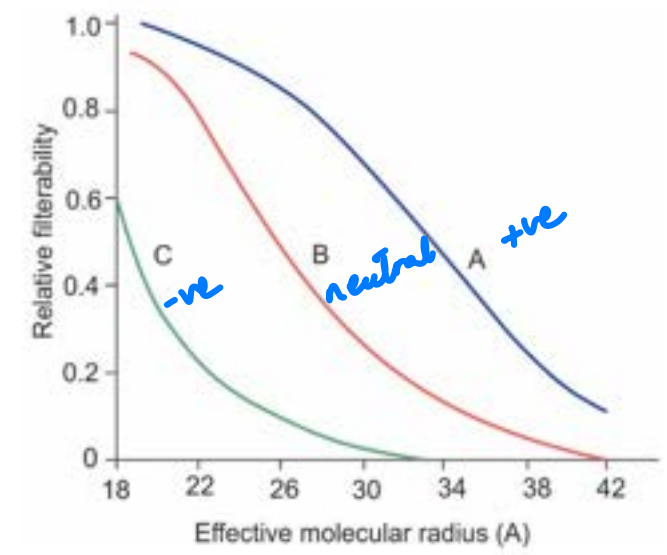
Cystometry
 Laplace's law: $P = \frac{2T}{R}$

Glomerular Filtration

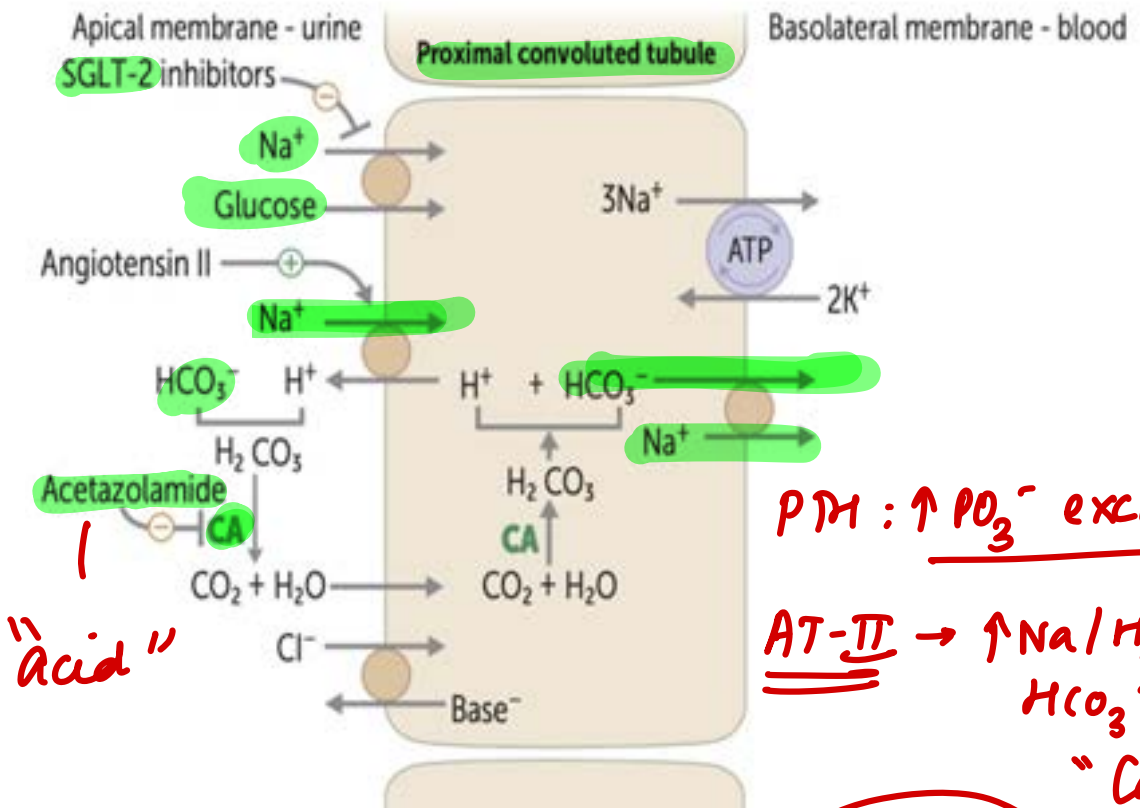


	GFR	RPF	FF $\frac{GFR}{RPF}$
<u>Afferent arteriole constriction</u>	↓	↓	-
<u>Efferent arteriole constriction</u>	↑	↓	↑
High plasma protein concentration	↓	-	↓
Low plasma protein concentration	↑	-	↑
Ureter constriction	↓	-	↓
<u>Dehydration</u>	↓	↓↓	↑

- Glomerular filtration barrier: **SIZE / charge**
- Fenestrated capillary endothelium: 50-100nm
 - Basement membrane with type IV collagen chains and heparan sulfate
 - Visceral epithelial layer consisting of podocyte foot processes



RENAL TUBULES



"acid"

60% water
glc / HCO₃ / urea
aa

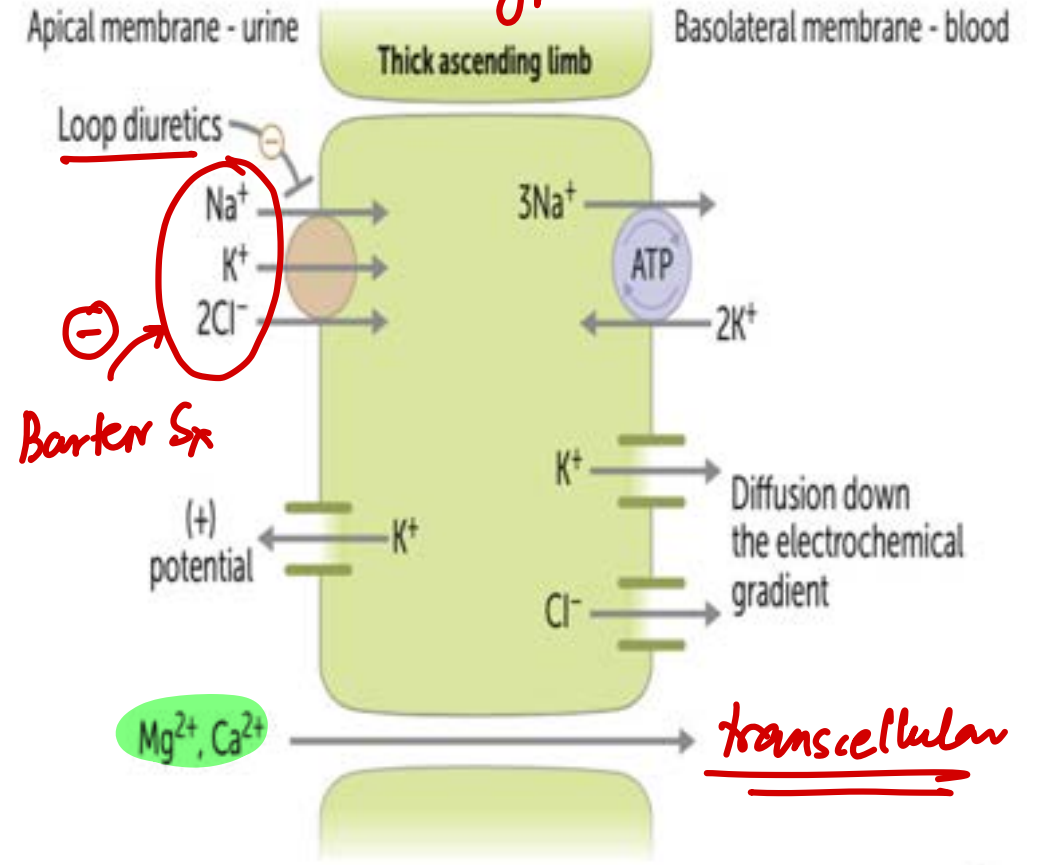
PTH : ↑ PO₄⁻ excretion

AT-II → ↑ Na/H₂O reabsⁿ
HCO₃⁻

"Contraction alkalosis"

isotonic

Hypotonic

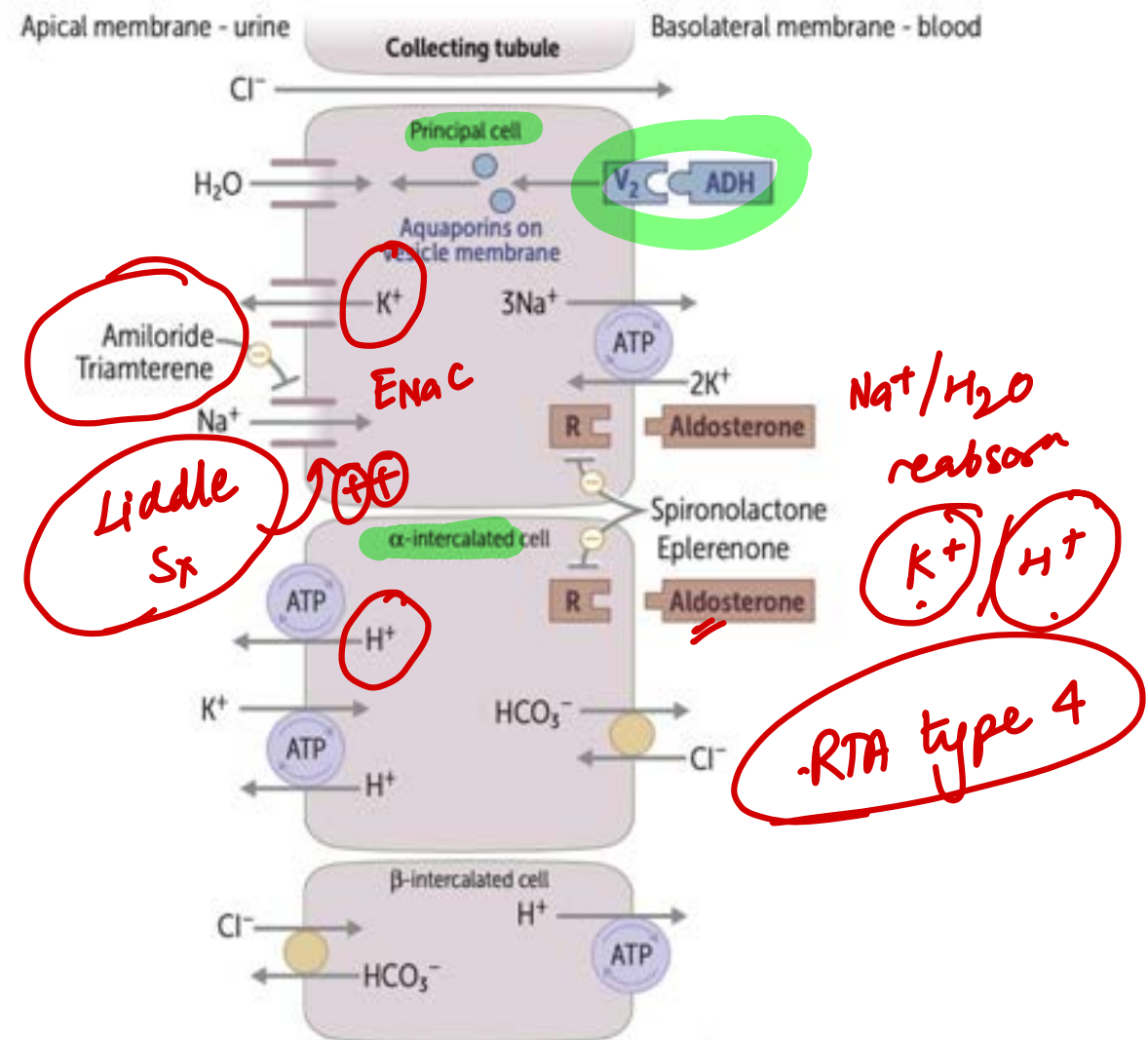
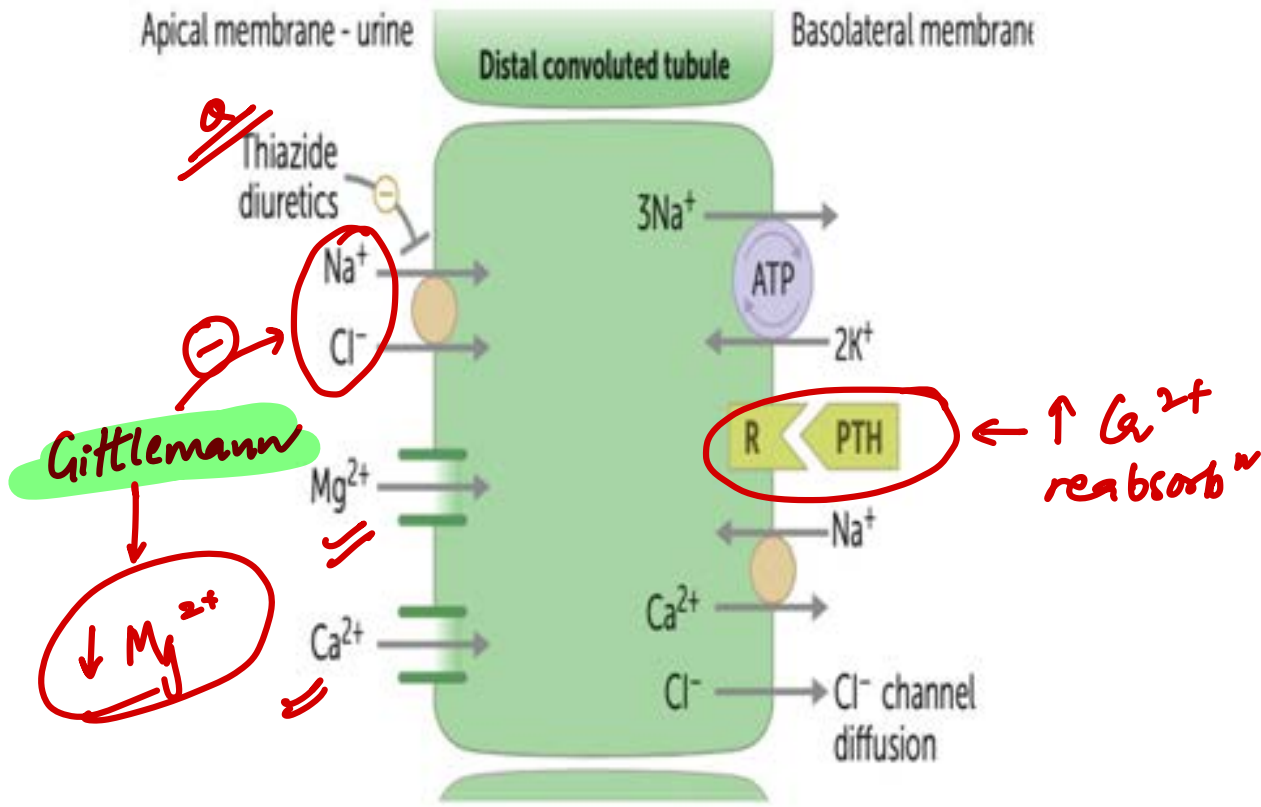


Bartter's

(+) potential

transcellular

THIN DESCENDING LOH: water only



1-2% water absorption: no ADH
 10% water absorption: ADH

DIURETICS-PHARMACOLOGY

Acetazolamide

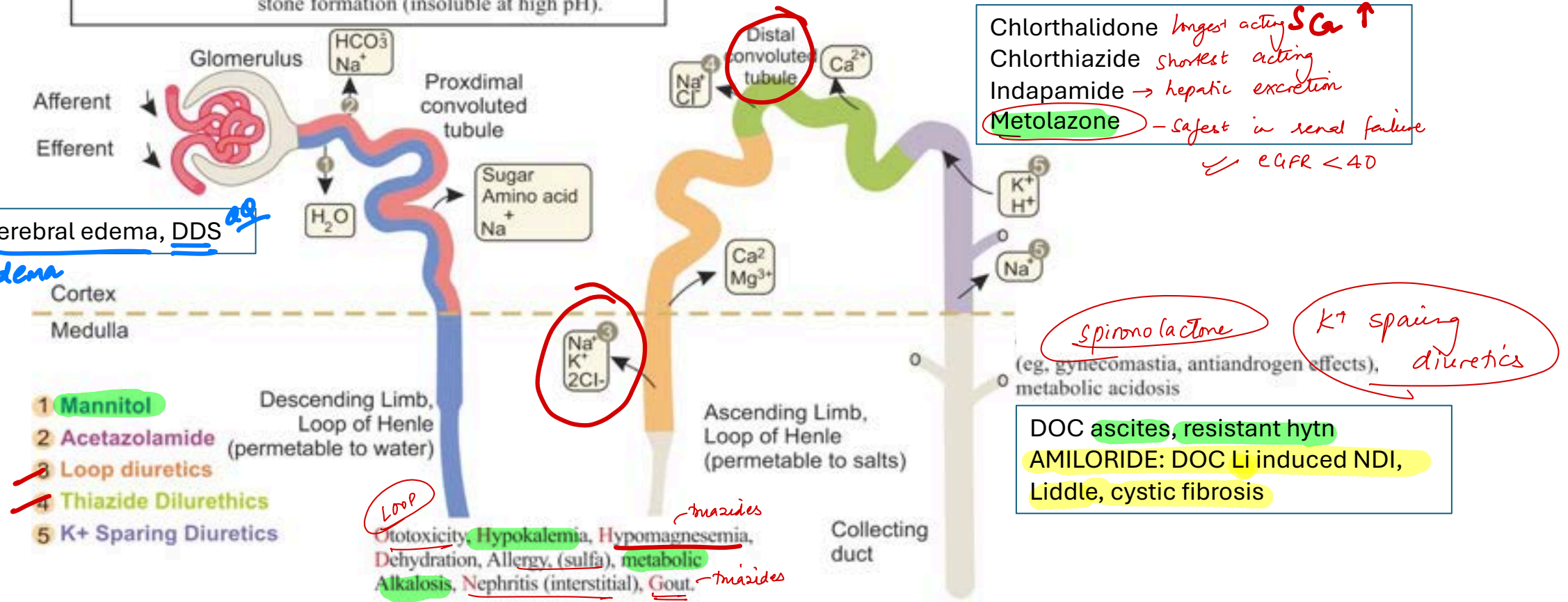
DOC in mountain sickness, can be used in familial hypokalemic periodic paralysis

ADVERSE EFFECTS Proximal renal tubular acidosis (type 2 RTA), paresthesias, NH₃ toxicity, sulfa allergy, hypokalemia. Promotes calcium phosphate stone formation (insoluble at high pH).

CLINICAL USE Hypertension, HF, idiopathic hypercalciuria, nephrogenic diabetes insipidus, osteoporosis

DOC ACG, Cerebral edema, DDS

CI - ♡ p. edema



Chlorthalidone longest acting Sca ↑
 Chlorthiazide shortest acting
 Indapamide → hepatic excretion
 Metolazone - safest in renal failure
 eGFR < 40

Spironolactone
 K⁺ sparing diuretics

DOC ascites, resistant hytn
 AMILORIDE: DOC Li induced NDI, Liddle, cystic fibrosis

- 1 Mannitol
- 2 Acetazolamide
- 3 Loop diuretics
- 4 Thiazide Diuretics
- 5 K⁺ Sparing Diuretics

Loop: Ototoxicity, Hypokalemia, Hypomagnesemia, Dehydration, Allergy, (sulfa), metabolic Alkalosis, Nephritis (interstitial), Gout.

Loops: Cardiogenic p.edema
 Torsemide: longest acting Sca ↓
 Bumetanide: most potent
 Ethacrynic acid: max ototoxicity.

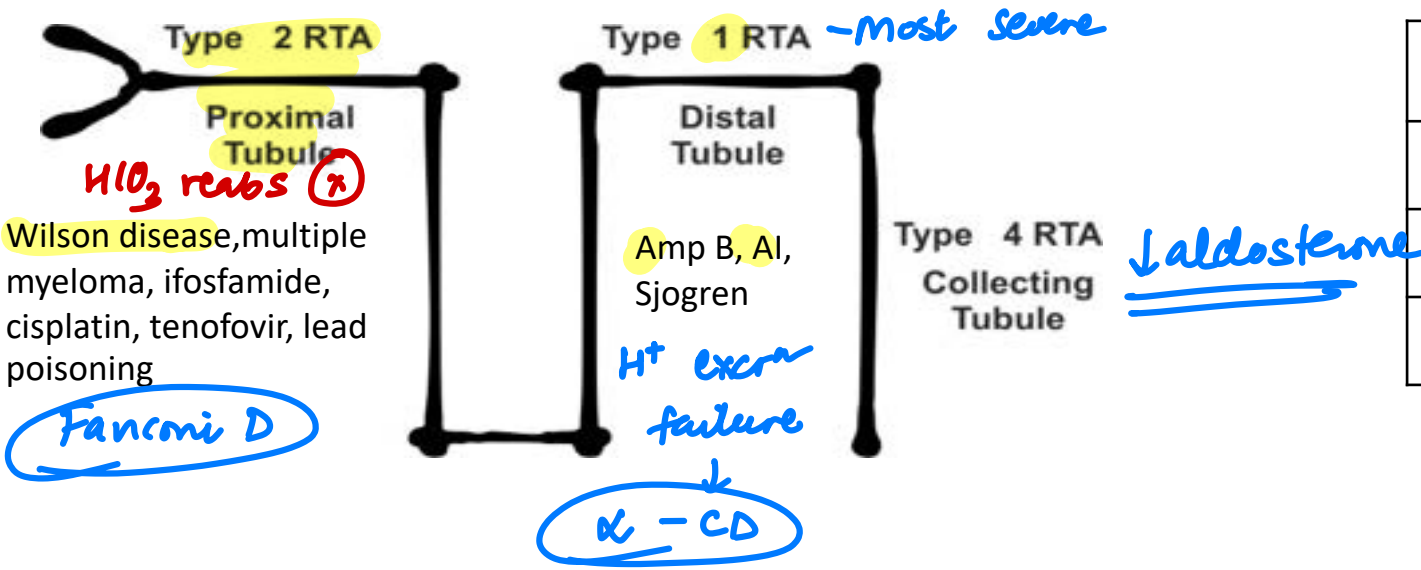
Spironolactone, Eplerenone, Amiloride, Triamterene,

Acidazolamide
↓ RR
Hypo K⁺
Acidosis

Thiazide
Loop D
↓
Hypo K
alkalosis

Spirochlorone
↓
Hyper K⁺
acidosis

TUBULAR DISORDERS



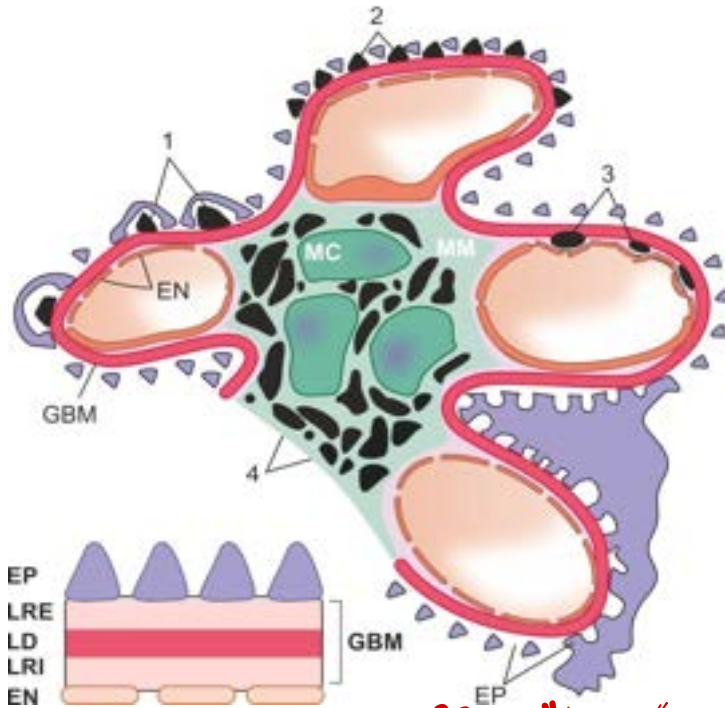
	K	Ca	Urinary pH	Nephrolithiasis
2	↓	↓	↓	⊖
1	↓	↑	↑	⊕⊕
4	↑	↓	↓	⊖

	TAL Na-K-2CL Loop	DCT Na-cl	CD ENac		
Dx	Barter's	Gittlemann	Gordon's	Pseudo hypo aldost	<u>Liddle Sx</u>
BP	↓	↓	↑	↓	↑
K ⁺	↓	↓	↑	↑	↓
P ^H	alkalosis	alkalosis	acidosis	acidosis	alkalosis
Ca ²⁺	Uca ↑ Sca ↓	Sca ↑ ↓ Mg ²⁺	-	-	-

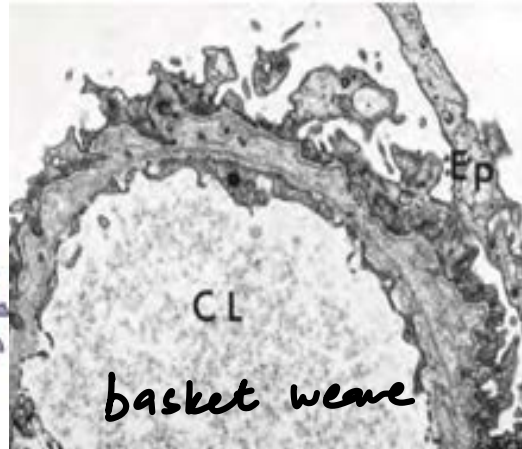
Hytn + ↓K⁺ + alkalosis

- aldosterone → Adenoma (Conn Sx)
 - Renin prod tumor
- Liddle Sx
- SAME → 11βHSD ⊖

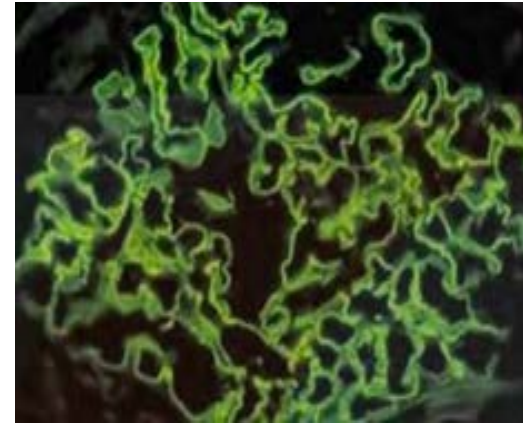
DEPOSITS



- 1- Sub epithelial < PSGN "humps"
Membranous "spike/dome"
- 2- Intra-membranous - MPGN type II
- 3- Sub-endothelial < MPGN type I
SLE nephritis
- 4- Mesangial - IgA / Berger's D

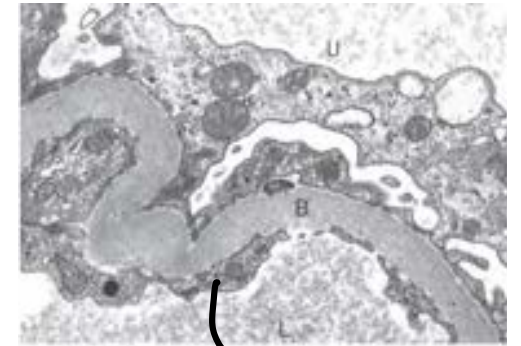
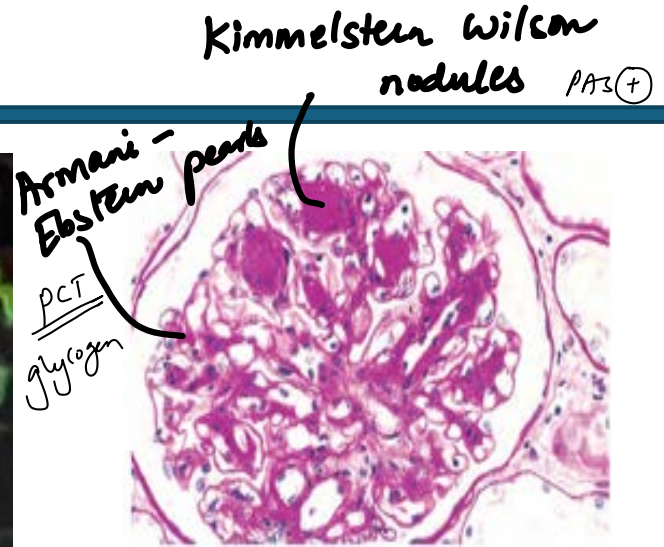
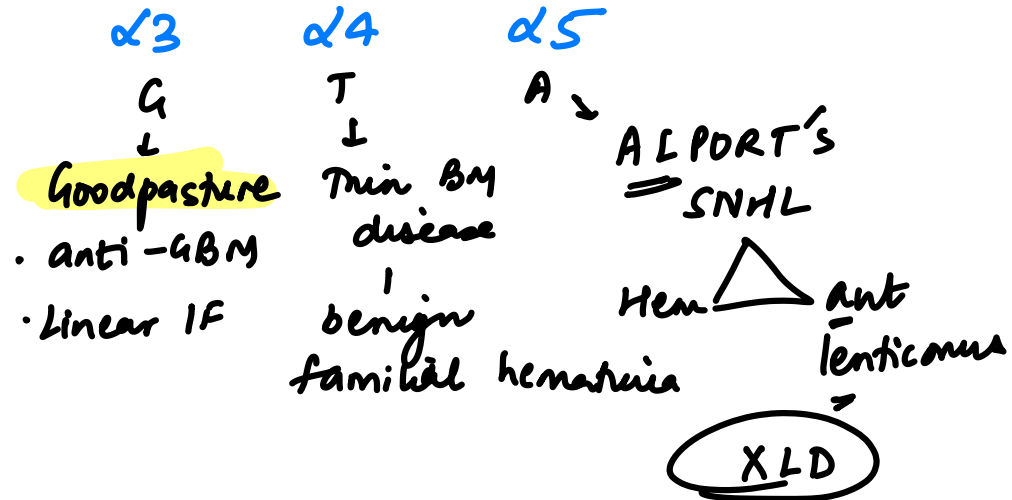


basket weave
ALPORT



Linear IF
Goodpasture

TYPE IV COLLAGEN



GBM thickening
↓
Hyperfiltration

Diabetes

NEPHRITIC SYNDROME

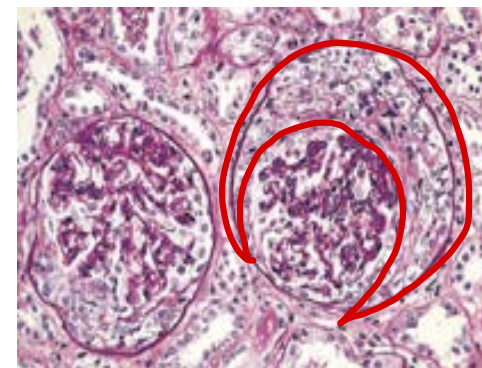
Buerger → TAO - smokers
=

Hematuria, Oliguria, Hypertension

Child -mc **PSGN**
 Hematuria 10-21d after pharyngitis/impetigo *S. pyogenes*
 (strain 12,4,1)
C3 transient low
 70% Anti-dsDNA+
 30% ASLO +

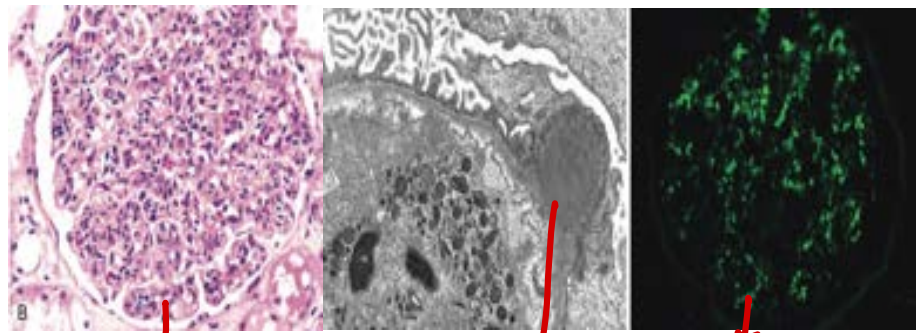
Adult -mc **IgA / Berger D**
 Hematuria 3d after pharyngitis
 Recurrent gross hematuria
C3 normal

Rapid progressive **RPGN**

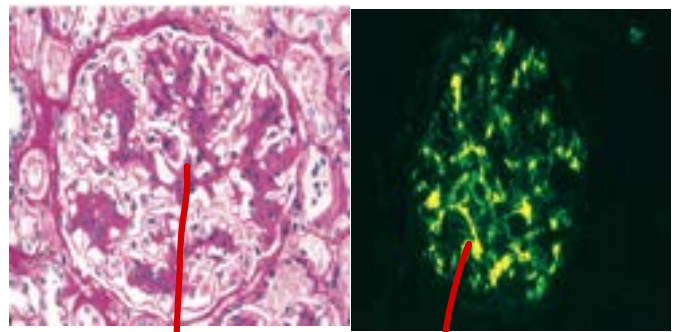


Crescents:
 • WBC
 • Fibrin
 • Parietal epithelial cells

Linear: Good pasture
 Granular: **PSGN**
 Pauci-immune: WG, MPA **anca+**



Hypercellular
 Subepithelial humps
 Granular IF "starry sky"



mesangial proliferations
 mesangial deposits

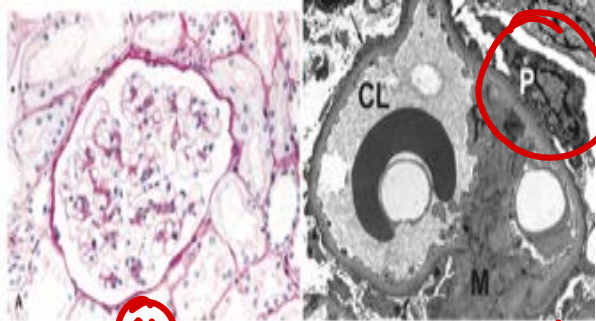
Sparsentan: **ARB** + Endothelin -

NEPHROTIC SYNDROME

Proteinuria >3g/d, Edema, frothy urine

Minimal change

Child -mc
 Prior URTI/
 immunisation
 NSAIDS, Hodgkin's
 lymphoma



(N) effacement of podocytes

Adults -mc
 Heroin
HIVAN: APOL1 polymorphism
 Reflux nephropathy
 Obesity
 Sickle cell anemia
NPHS2: Podocin-AR FSGS
Actinin 4: AD FSGS
TRPC6: Adult FSGS

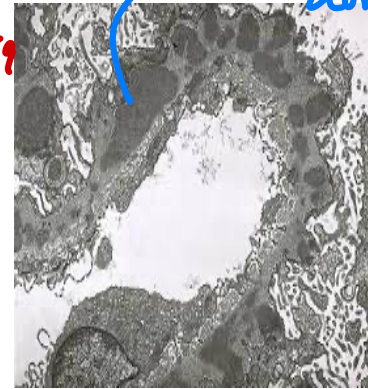
FSGS



Collapsing -> HIV -> COVID-19

Membranous

MC in elderly
 Adenoca lung / colon/
 melanoma
PLAR2
Thrombospondin, CD10



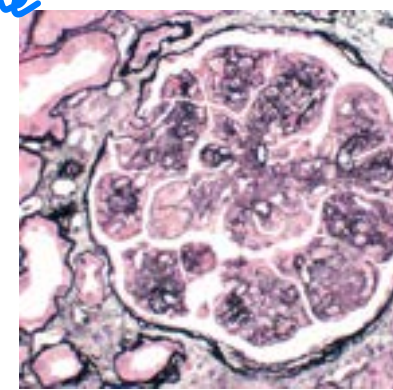
Subepithelial dome

MPGN

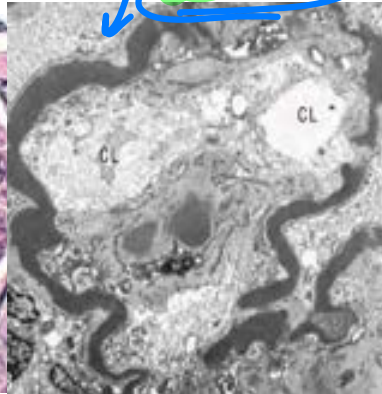
Adult
 HBV/HCV /malaria

type 1:
 subendothelial

type 2:
 membranous
C3NEF



tram-track

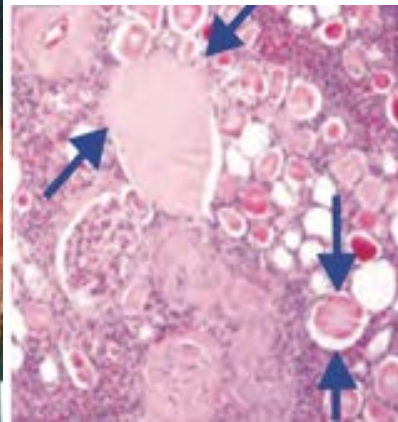
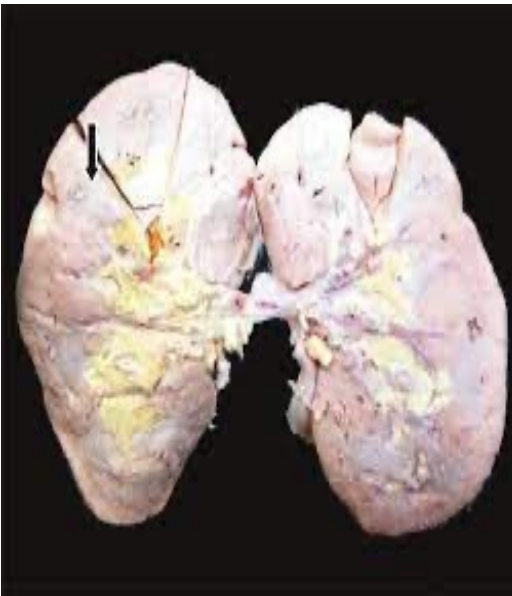


thickening
 wavy
 GBM

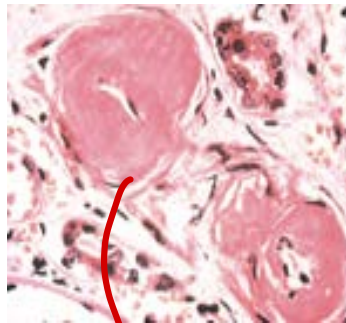
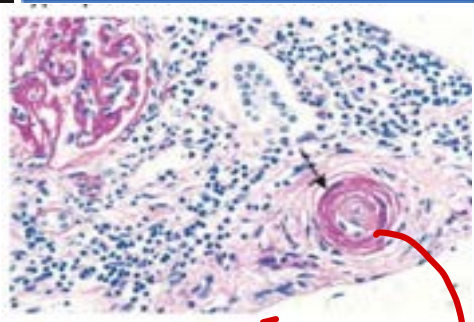
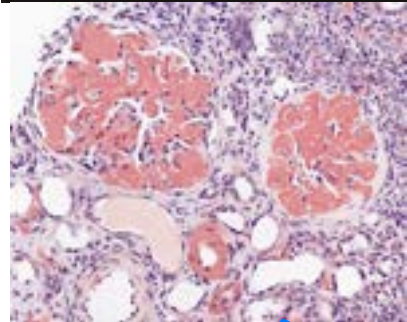
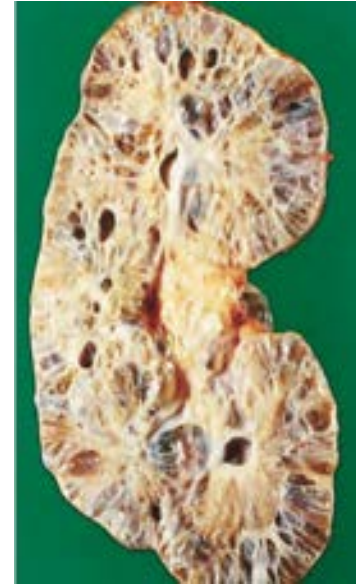
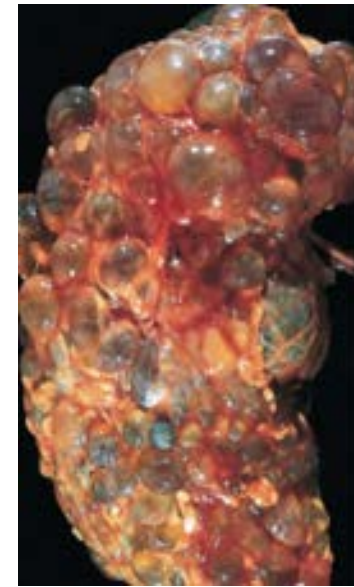
SRNS: 4wks of Rx -> 8z
 DOC: **TACROLIMUS**
Steroid dependent NS:
MMF severe
 Cyclophosphamide >8yrs
 Levamisole mild

Nephrin NPHS1-Finnish type: Congenital NS

Renal pathology



Chronic PN
"thyroidization of tubules"



waxy kidney
Amyloidosis ↑mc
AL → Bence Jones

Flea bitten
↓
RPGN
PSGN
Malignant htn

Leather grain
Hyaline arteriosclerosis
DM

Chr 16,4: PKD1 and 2
Polycystin

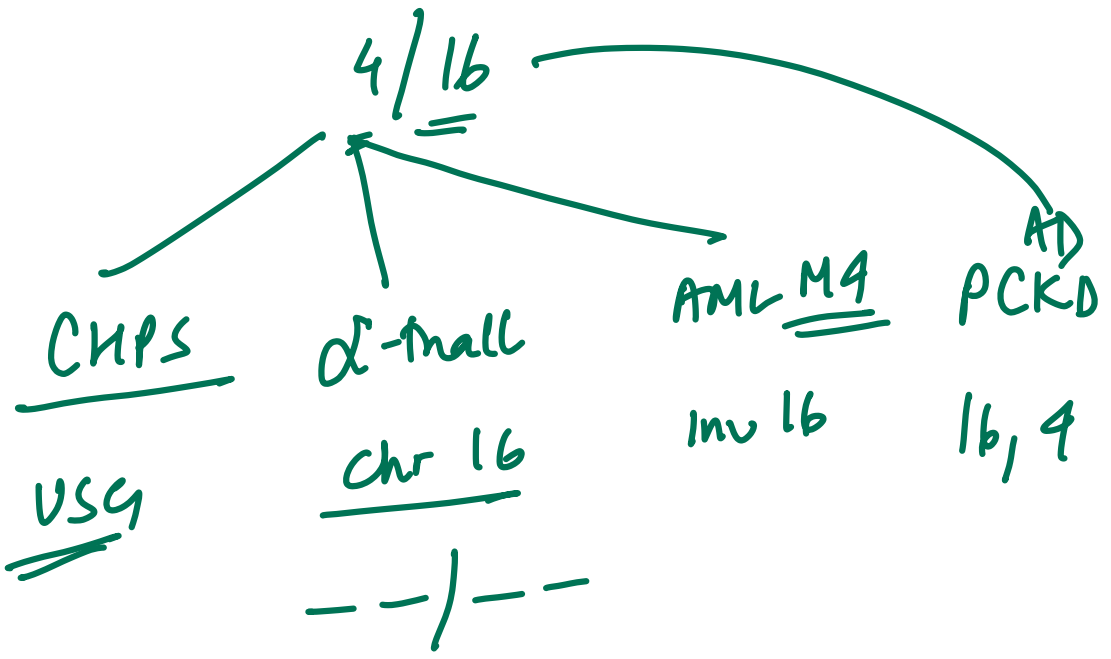
Aortic dissection
Berry aneurysm
Diverticulosis MVP

• AD - PCKD
• adults

Chr 6: PKHD
Fibrocystin

Congenital hepatic fibrosis or

• AR PCKD
• end stage
"infancy"

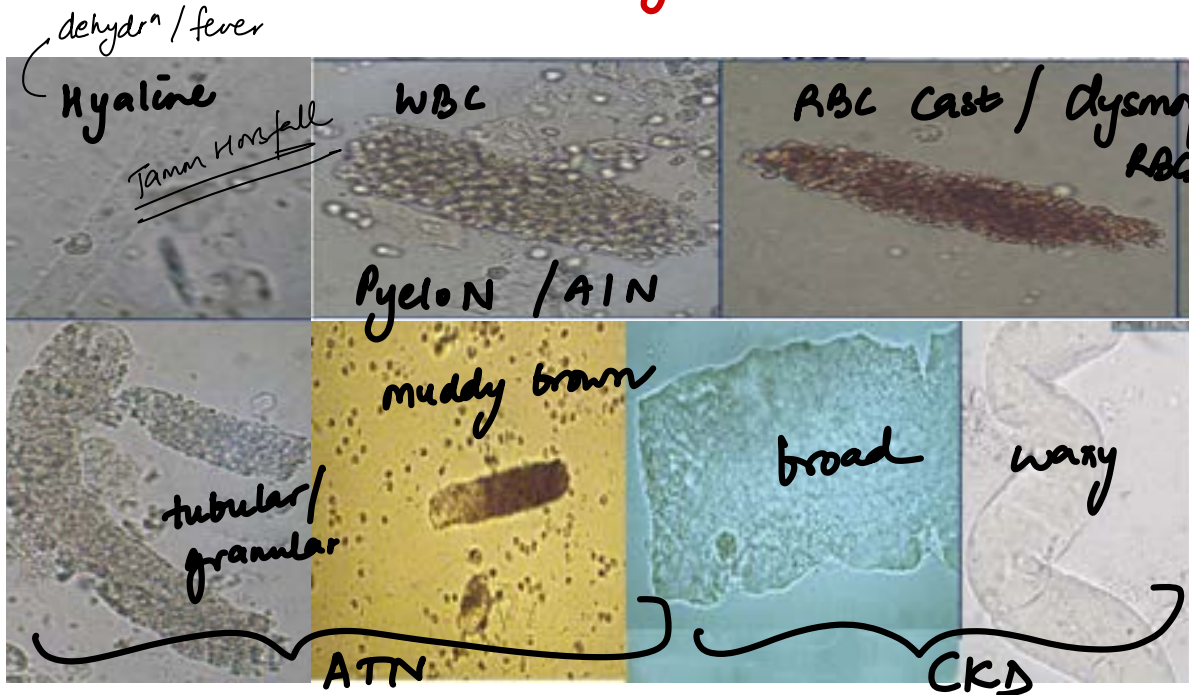


AKI VS CKD

	AKI	CKD
CMD	preserved	lost
SIZE	(N) / ↑	Contracted
URINE OSMOLARITY	variable	1.010 isosthenuria
ANEMIA	-	EPO deficiency
MBD	-	(++)
CASTS	Hyaline / tubular (+)	broad / waxy

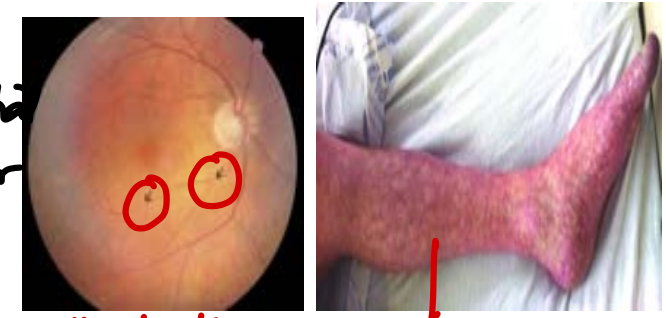
Biomarkers of AKI:
 Cystatin C
 KIM-1
 NGAL
 TIMP2
 IGFBP7

Renal papillary necrosis:
 NSAIDS
 Sickle cell disease or trait
 Acute pyelonephritis
 Infections - TB
 Diabetes mellitus



AKI

	Pre renal	Acute Tubular necrosis	GN
Cause	Hypovolemia, CHF, NSAID / ACE- / HRS	Sepsis, Ischemia, Nephrotoxins: Rhabdomyolysis, IVH, Tumor lysis syndrome, <u>MM</u> , Drugs, Iodinated contrast	Interstitia tubular
Fractional excretion of Na	<1%	>1%	
Urine Na	<10 meq/L	>20 meq/L	
Urine Osmolality	>500	<350	
BUN/Creatinine	>20:1	<10:1	
Urine casts	Hyaline	Granular / muddy brown	



- Hollenhorst plaques + Livedo reticularis
 - ATN → Atheroembolic D
- Fever + Rash + Eosinophilia + Drugs : **AIN**^{aa}
- ↓
- NSAIDs MC

RIFLE / KDIGO / AKIN

Risk KDIGO Stage 1	EGFR Decrease by 25% Creatinine Increase by 1.5x	UO <0.5 mL/kg/hour for 8 hours
Injury KDIGO Stage 2	EGFR Decrease by 50% Creatinine Increase by 2x	UO <0.5 mL/kg/hour for 16 hour
Failure KDIGO Stage 3	EGFR Decrease by 75% Creatinine Increase by 3x	UO <0.3 mL/kg/hour for 24 hour or anuric for 12 hour
Loss	Persistent renal failure > 4 weeks	-
End stage	Persistent renal failure >3 months	-

CKD

Stage of CKD	eGFR result
Stage 1	90 or higher
Stage 2	60-89
Stage 3a	45-59
Stage 3b	30-44
Stage 4	15-29
Stage 5	less than 15

reversible

complicat

-prepare

-RRT

MCC of death: *CVC causes - accelerated*
 Anemia: *EPO deficiency* → *R₂-EPO* → *arteriosclerosis*
 Bone disease: *Id OH* ↓ *Ca²⁺* ↑ *PTH* 2° ↑ *PO₄* ↑ *ALP* → *s/e: Hytn* 10-11.5
 Calciphylaxis: *Ca-PO₄*
 Acid-base: *NA GMA* → *HA GMA*
 Uremia:
 Pericarditis
 P. Edema
 Ph < 7.2
 Potassium > 6.5
 Encephalopathy

dialysis

Dialysis disequilibrium syndrome DOC: Mannitol



blood vessels



Rugger Jersey spine

Acid-base imbalance

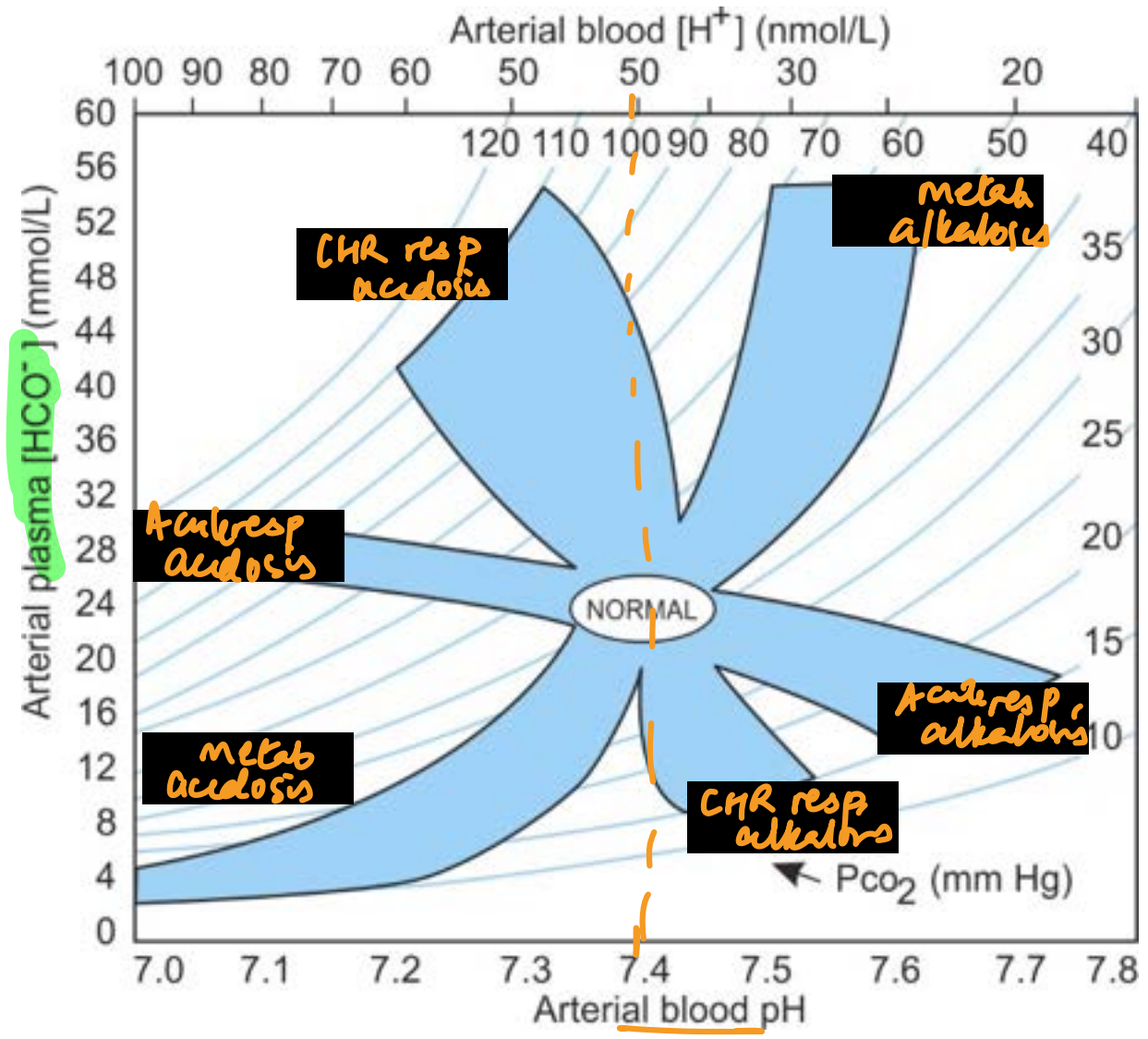
pH - 7.4
Co2 - 40mm
HCo3- 29 meq/L

	pH	PRIMARY CHANGE	COMPENSATION
METABOLIC ACIDOSIS	↓	<u>HCO₃</u> ↓	CO ₂ ↓
METABOLIC ALKALOSIS	↑	HCO ₃ ↑	<u>CO₂</u> ↑
RESPIRATORY ACIDOSIS	↓	CO ₂ ↑	<u>HCO₃</u> ↑
RESPIRATORY ALKALOSIS	↑	<u>CO₂</u> ↓	<u>HCO₃</u> ↓

Winter's formula

$$P_{CO_2} = 1.5[HCO_3] + 8 \pm 2$$

Acid-base imbalance



On laboratory investigations in a patient, $\text{pH}=7.3$, $\text{pCO}_2=35$ mm Hg, What is the likely acid base imbalance?

A. ~~Respiratory~~ acidosis

~~B. Metabolic~~ acidosis

C. ~~Metabolic~~ alkalosis

D. ~~Respiratory~~ alkalosis

A patient is having pH-7.12, HCO_3^- -28 and PCO_2 -50 mm Hg. What is the acid base disorder in this patient?

A. Metabolic acidosis with respiratory compensation

B. Metabolic alkalosis with respiratory compensation

C. Respiratory acidosis with renal compensation

D. Respiratory alkalosis with renal compensation

A patient is having pH-7.27, HCO₃-14 and PCO₂-28 mm Hg. What is the acid base disorder in this patient?

A. Metabolic acidosis with respiratory compensation

B. Metabolic acidosis with respiratory acidosis

C. Metabolic acidosis with respiratory alkalosis

D. Respiratory alkalosis with renal compensation

$$1.5 \times \text{HCO}_3 + 8 \pm 2$$

$$1.5 \times 14$$

$$= 21 + 8 \pm 2$$

$$= 29 \pm 2$$

$$\neq 27 - 31$$

pO₂ → 34 mm

~~pO₂ - 25 mm~~

A patient who is a known case of CKD has complaints of vomiting. His ABG reports are as follows: pH-7.40, pCO₂- 40, HCO₃⁻-25. Na-145, chloride-100. What is the metabolic abnormality?

A. Normal anion gap metabolic acidosis

B. High anion gap metabolic acidosis

C. No acid base abnormality

D. High anion gap metabolic acidosis with metabolic alkalosis

ANION GAP

$$145 - (100 + 25)$$

20

High Anion-Gap Metabolic Acidosis

Anion Gap: 12+/-4

• Anion gap = $(Na +/- K) - (HCO_3 + Cl)$

NAGMA = Hyperchloremic acidosis:

Causes of NAGMA	
• Renal tubular acidosis	VAG (+)
• Diarrhea	
• Carbonic anhydrase inhibitors	
• Ureteral diversion (e.g., ileal loop)	

High anion gap metabolic acidosis

Associated clues

Drug ingestion Hypoperfusion Renal failure Hyperglycemia Osmolal gap

↑ Serum lactic acid

↑ Blood urea nitrogen

Urine & serum ketones

Salicylate

Lactic acidosis

Uremia

DKA

Methanol

Ethylene glycol

Resp alkalosis + NAGMA

- Hooch tragedy
- Formic acid
- Retinotoxic

- Ca oxalate crystals
- anti-freeze

Antidote: Fomepizole

ELECTROLYTES

Serum osmolarity: $2(\text{Na}) + \text{glucose}/18 + \text{BUN}/2.8$

$\downarrow \text{Na}^+$

Sodium deficit: $\text{TBW} \times (\text{Desired} - \text{Actual})$

TBW: $0.6 \times \text{Body weight}$

Max: 8 meq/l in a day

$\uparrow \text{Na}^+$

Free water deficit

$$= \frac{\text{Na} - 140}{\text{Na}} \times \text{TBW}$$

The serum electrolyte values of a patient weighing 60kg are given below. Calculate the sodium deficit in the patient. pH: 7.42, Na⁺: 120 mEq/L, serum K⁺: 4 mEq/L, serum Cl⁻: 90 mEq/L?

A. 20 mEq

B. 400 mEq

C. 200 mEq

D. 720 mEq

TBW \times Des-Act

\downarrow

$$\frac{60}{100} \times 60 \times \frac{140 - 120}{1}$$

$$\frac{60 \times 60 \times 20}{100}$$