INTEGRATED RENAL-ELECTROLYTES

Renal Physiology

Clearance= $\frac{U_x V}{P_x}$ (ml/min)

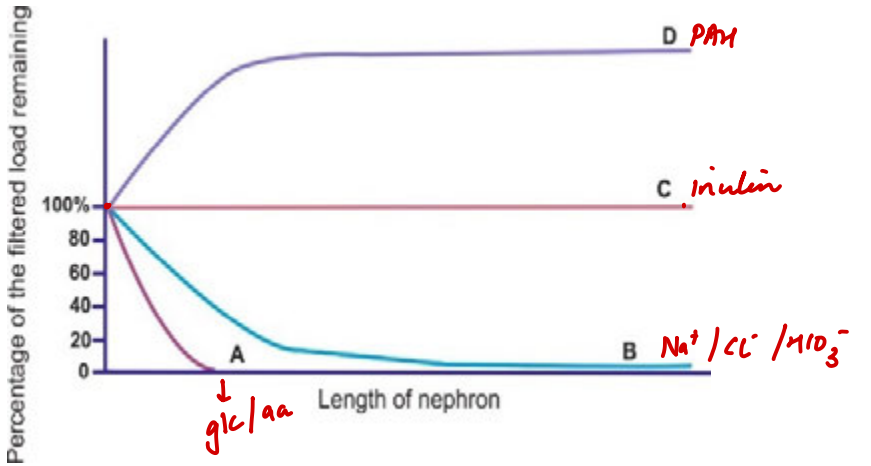
GFR= C_{inulin}

RPF= C_{PAH} $\quad RBF = \frac{RPF}{1-Hct}$

Filtration fraction= $\frac{GFR}{RPF}$ ~20%

Clearance: **PAH** > Creatinine > **Inulin** > Urea > Na > Glucose

(PAH: secrn; Creatinine: over-estimates the GFR; Urea, Na, Glucose: reabsorbed)

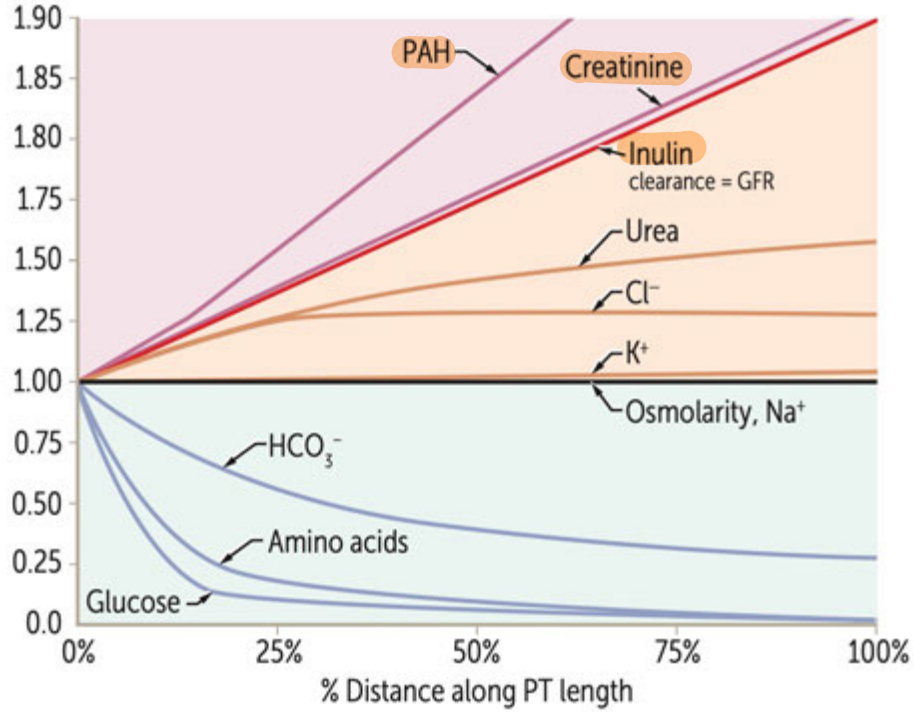


Counter-current :

CC multiplier – LOH (main)

CC exchanger: (maintains) – Vasa recta

Macula Densa	JG apparatus	Juxtaglomerular cells
- chemosensor - TAL–DCT jn - Na^+ ↑ → adenosine → afferent arteriole VC → GFR ↓ tubulo-glomerular feedback		Lacis cells - baroreceptor - mod. smooth muscle cells in afferent arteriole Glomerulo-tubular feedback ↓ GFR → RENIN → RAAS B_1 Na^+ / H_2O reabsorption K^+ / H^+ excr

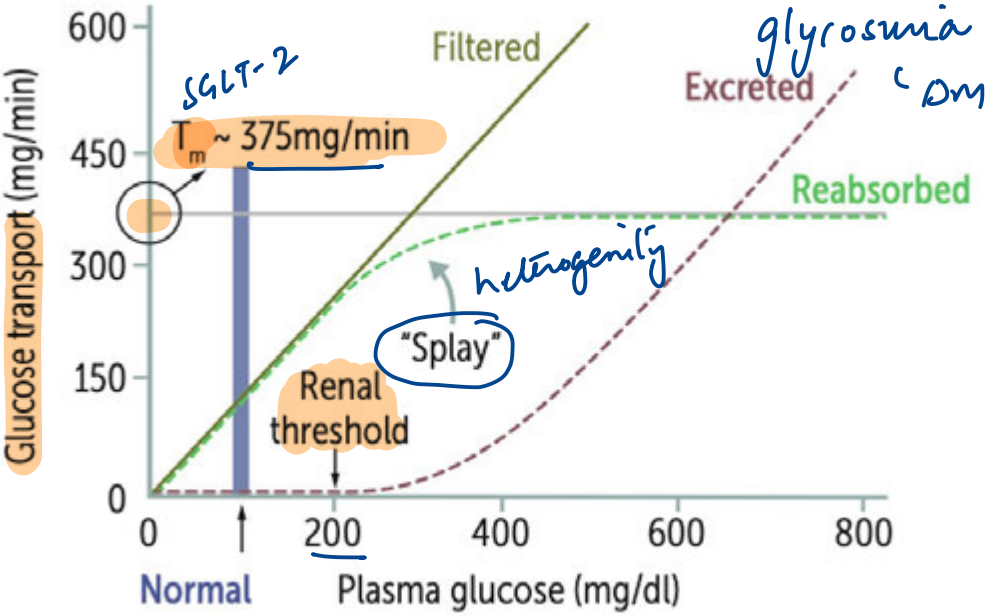


Angiotensinogen → Angiotensin -I
renin
↓ ACE → breakdown bradykinin

AT-II

- VC
- "ACE"
  - AT II constricts efferent
  - GFR ↑
- PCT
  - ↑ Na^+ / H_2O /
  - HCO_3^- reabsorption
  - "contraction alkalosis"
- Aldosterone
  - Na^+ / H_2O reab
  - K^+ / H^+ excr
- ADH

ADH
- V1 → VC
- V2 → CO - ↑Ag 2
  - VWF release / f8
- V3 → ↑ACTH (ant pit)

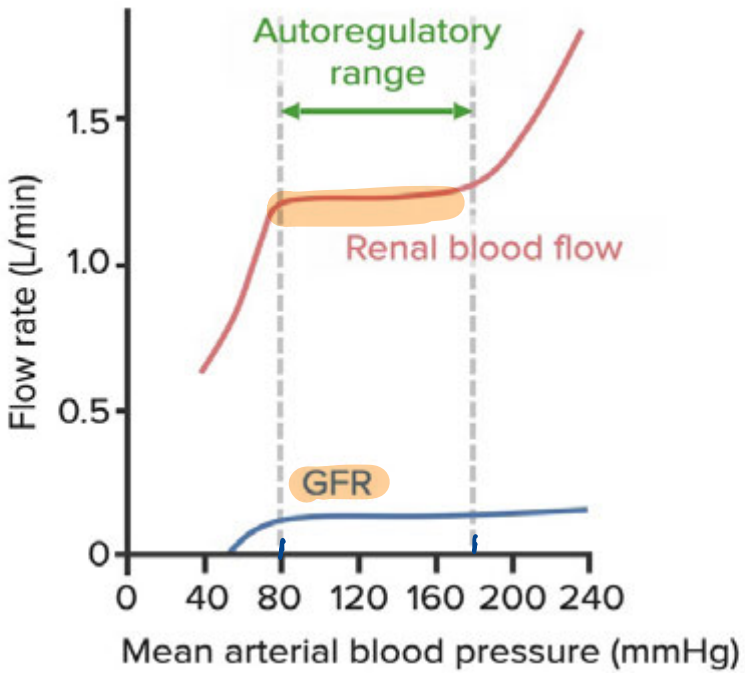


SGLT-2

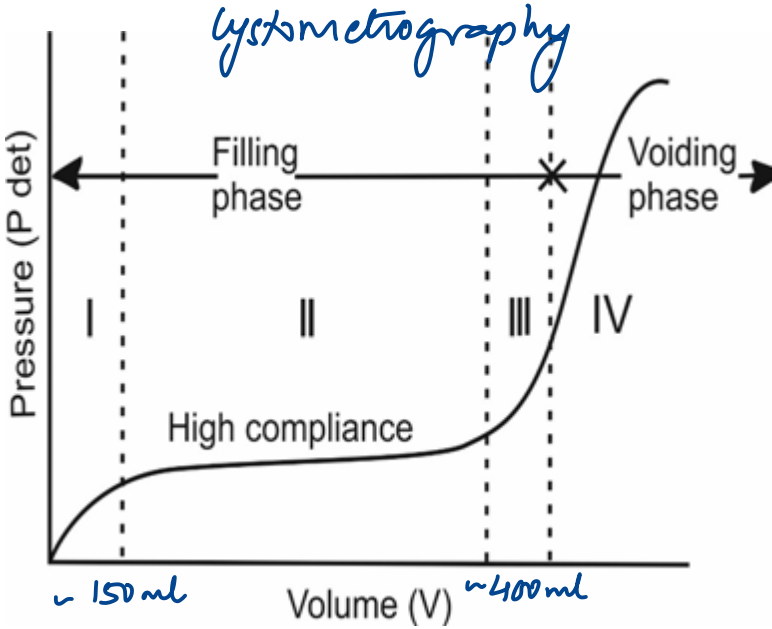
glycosuria (DM)

heterogeneity

Pregn - ↑plasma vol.
↳ physiological glucosuria



80 - 180 mm Hg

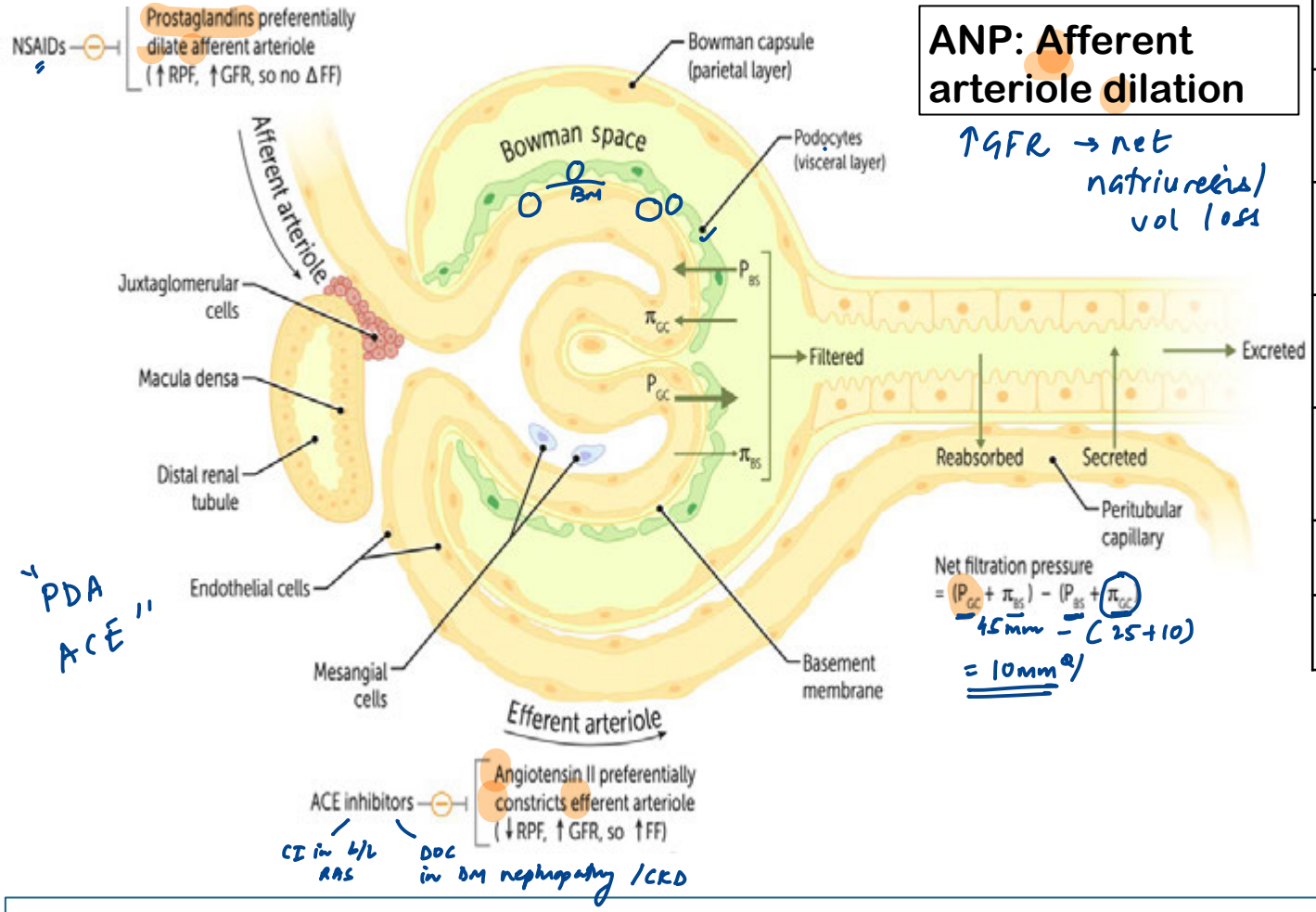


Laplace law =

$$P = \frac{2T}{R}$$

- parasymp → "pee" → detrusor contract
  IUS relax
  EUS → somatic
  ↳ S2-S4 pudendal N
- symp → "stores" - detrusor relax

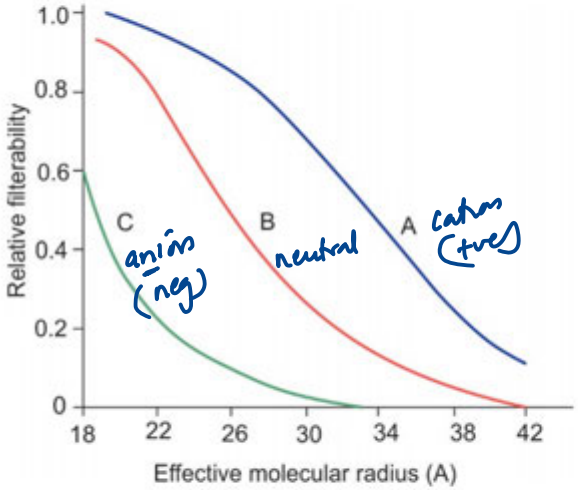
Glomerular Filtration



ANP: Afferent arteriole dilation

↑GFR → net natriuresis/vol loss

	GFR	RPF	FF
Afferent arteriole constriction	↓	↓	–
Efferent arteriole constriction	↑	↓	↑↑
High plasma protein concentration	↓	–	↓
Low plasma protein concentration	↑	–	↑
Ureter constriction – post-renal AKI	↓	–	↓
Dehydration	↓	↓↓	↑

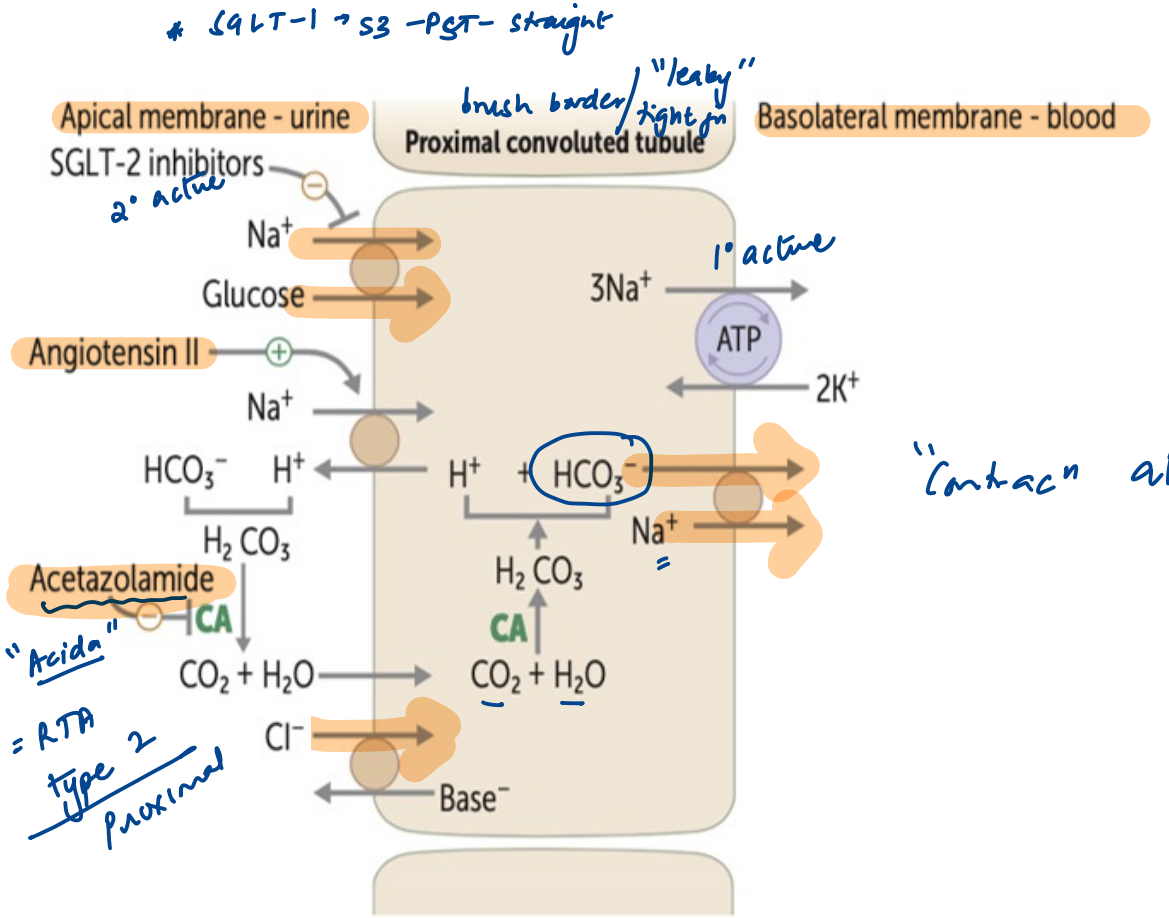


Glomerular filtration barrier:

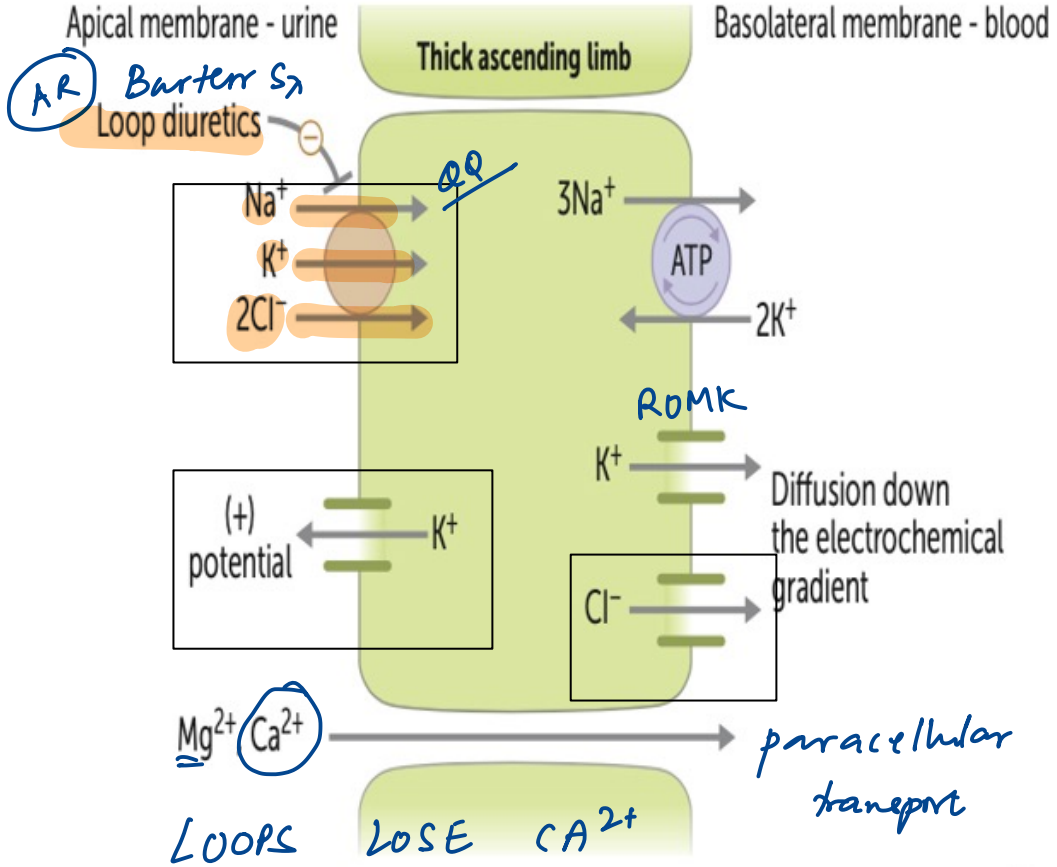
- **Fenestrated** capillary endothelium: 50-100nm – size → neg charge
- Basement membrane with type IV collagen and **heparan sulfate**
- Podocyte **foot processes** Slit diaphragm pore size: ~ 4 nm – size

Dopamine **A**NP **N**O **c**AMP **PGE2** – mesangial relaxation → ↑GFR

Renal tubules



"Contract alkalosis"

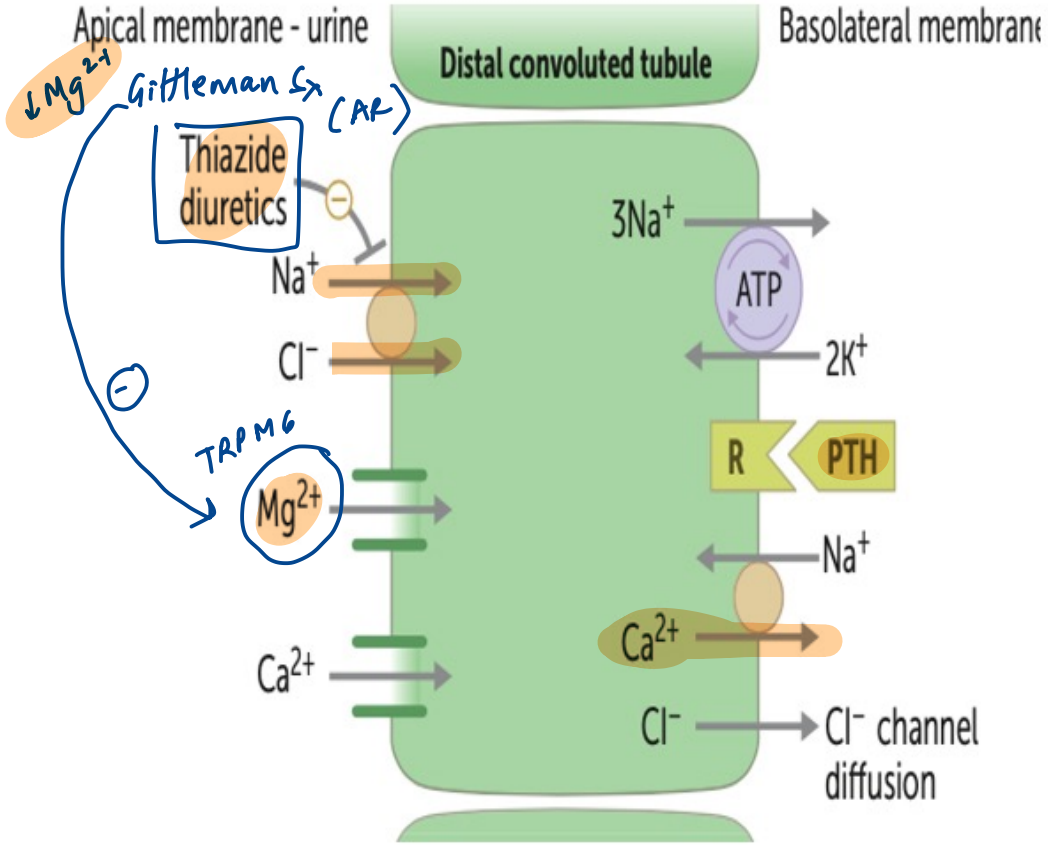


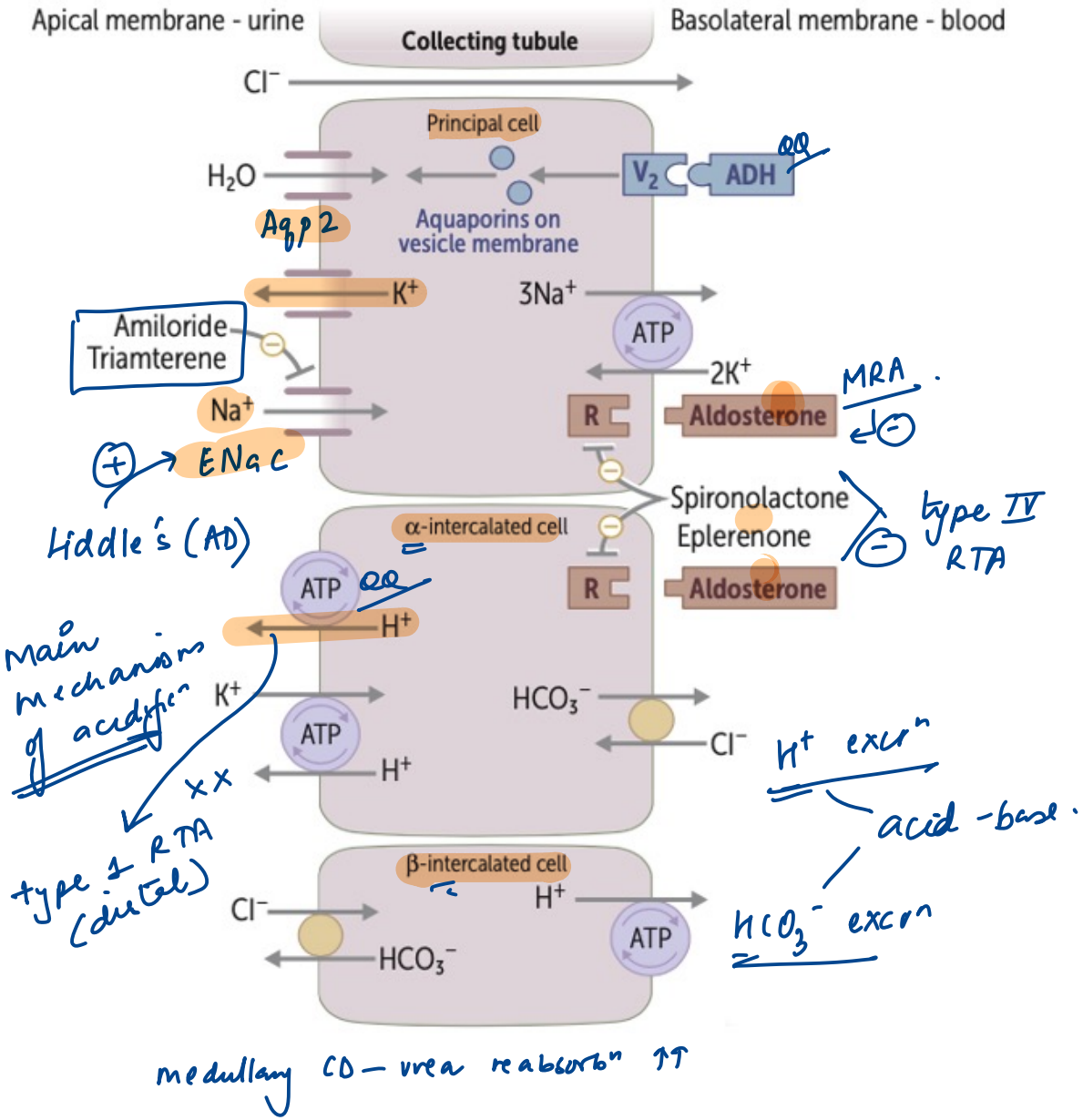
LOOPS LOSE CA^{2+}

- 60% water — AQP 1 max
- max Na^+ / Cl^- reab / HCO_3^- except Mg.
- 100% glc / aa
- NH_3 excn — allows more H^+ excn

PTH:
PCT: PO_4 excn ↑
DCT: Ca^{2+} reabsorpn ↑

THIN DESCENDING LOH: H_2O reabsorpn (→ concentrating segm)



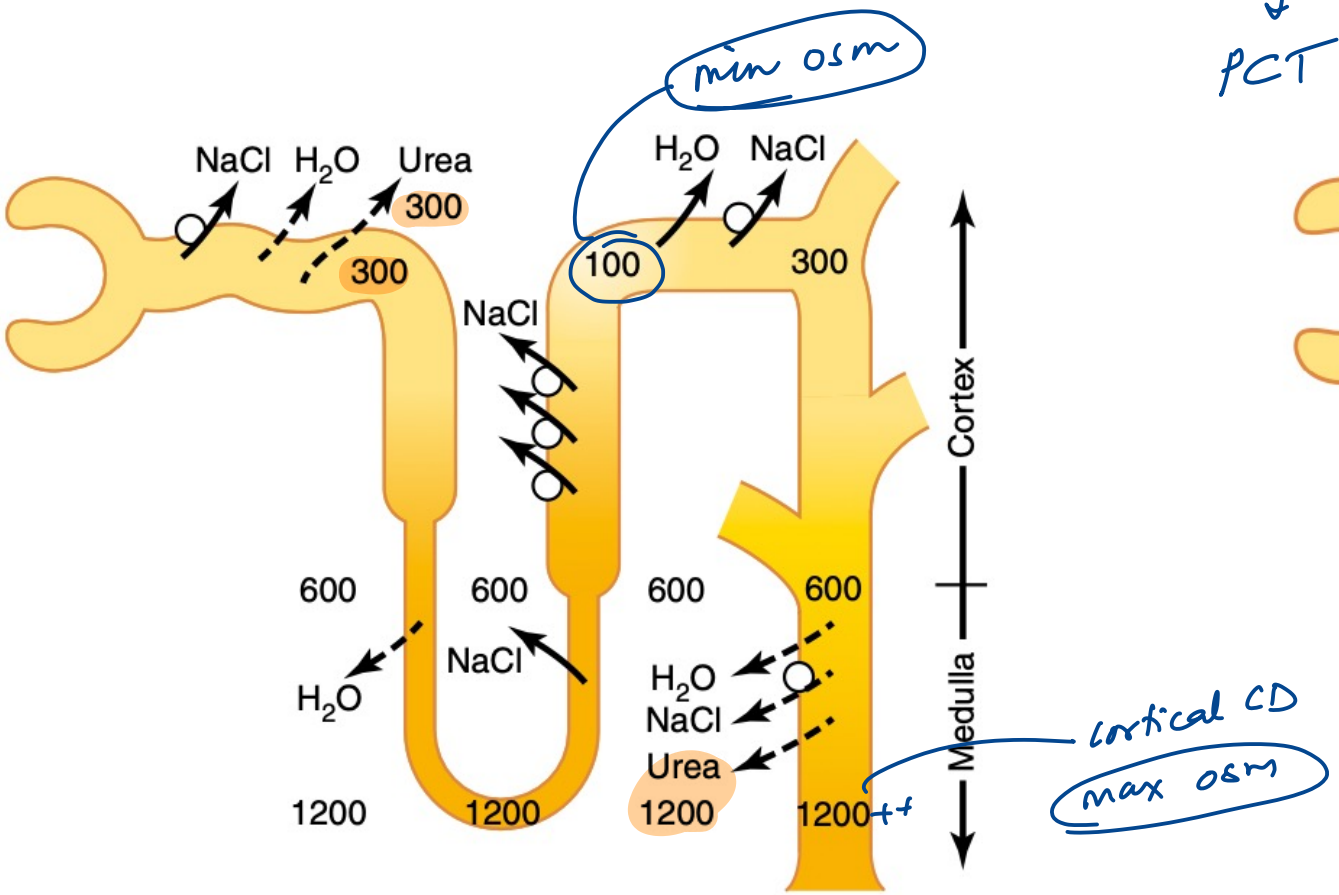


1-2% water absorption: no ADH
10% water absorption: ADH

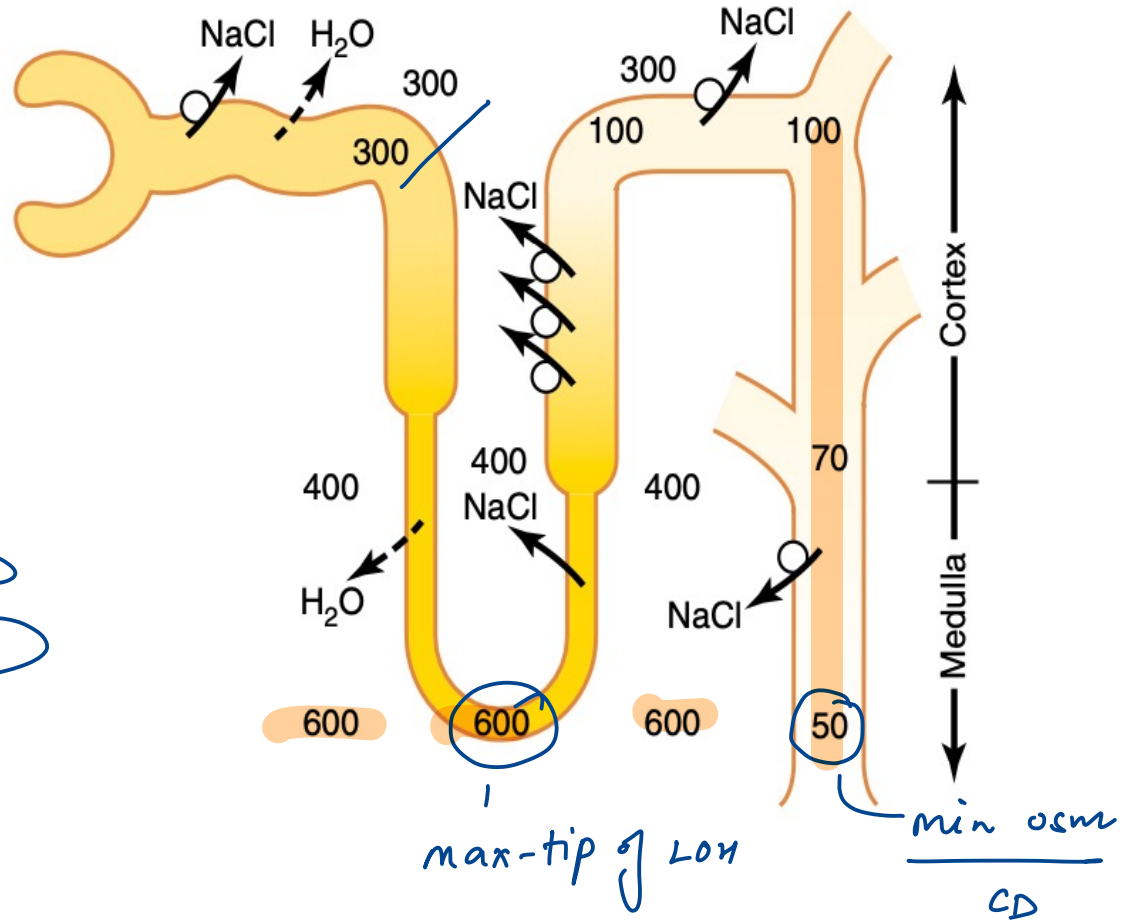
The story of ADH

max H_2O reabsorn
↓
PCT

ADH normal



Absent ADH



Diuretics Pharmacology

Acetazolamide

S/E:
- Type 2 RTA
- Paresthesias
- NH3 toxicity
- Sulfa allergy
- Hypokalemia
- Calcium phosphate stones (insoluble at high urine pH) – alkaline pH urine

DOC
- mountain sickness
- Familial hypokalemic PP

resp alkalosis

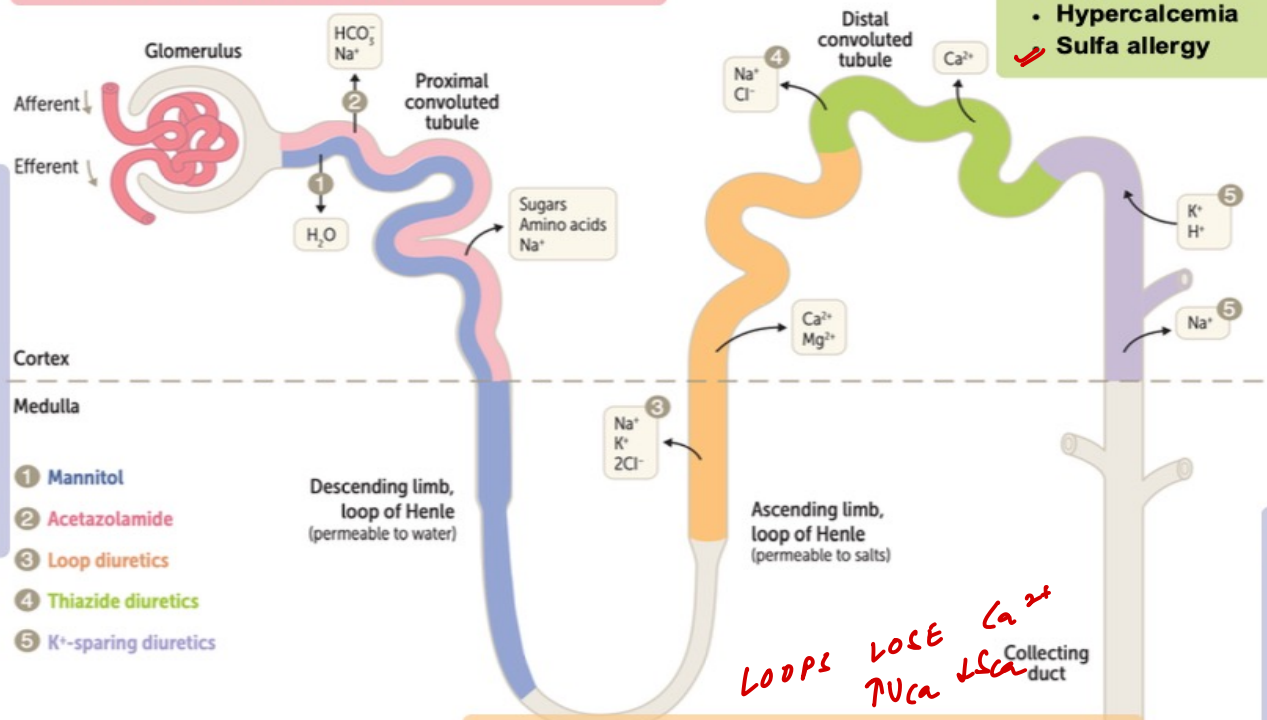
Thiazide

S/E:
- Metabolic alkalosis
- Hyponatremia
- Hyperglycemia
- Hyperlipidemia
- Hyperuricemia
- Hypercalcemia
- Sulfa allergy

Chlorthalidone - longest
Chlorthiazide - shortest
Indapamide - Liver excrn
Metolazone safest in renal failure

SCa↑ UCa↓

DOC / osteoporosis / ↑Calciuria



DOC:

ACG, DDS
Cerebral edema

Mannitol osmotic diuretic

S/E:
-Dehydration
-Hypo- or hypernatremia
-Pulmonary edema

C/I: Anuria, HF

Loop Diuretics

S/E:
- Ototoxicity
- DehydrationAllergy
- Sulfa allergy
- Metabolic Alkalosis
- Interstitial Nephritis
- Gout

Loops: Cardiogenic p.edema (ceiling effect)

Torsemide: longest acting
Bumetanide: most potent
Ethacrynic acid: max ototoxicity ↳non-sulfa

LOOPS LOSE Ca2+ ↑UCa ↓SCa

Potassium Sparing

S/E:
- Hyperkalemia
- Metabolic acidosis

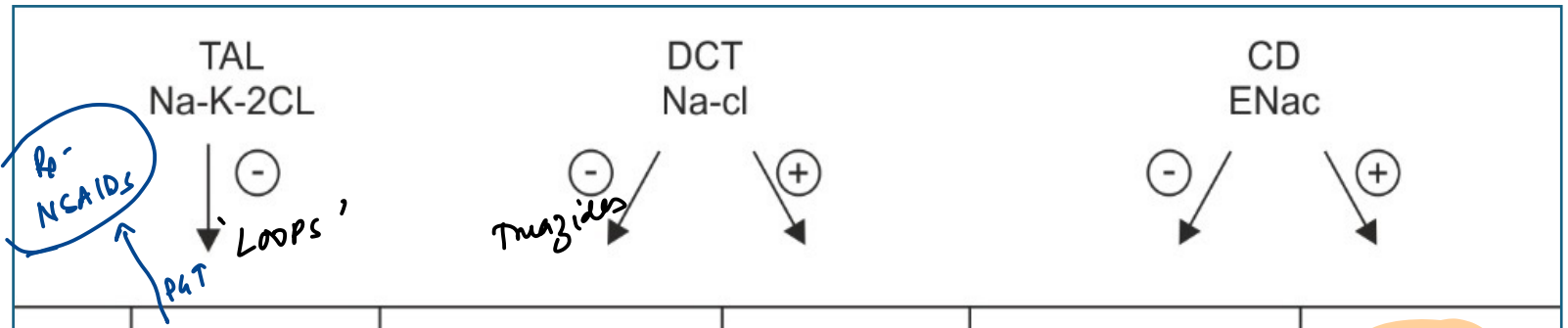
MRA:
DOC ascites, resistant HtN

AMILORIDE:
DOC Li induced NDI, Liddle, cystic fibrosis

SEAT
- MRA: ↑ gynecomas
  - Spironolactone ♂↑
  - Eplerenone ♂↑
  - Finerenone ♂=♀ (non-steroidal)
- ENa c ⊖
  - Amiloride
  - Triamterene

Lorundrostat (Refractory hyTn) — aldosterone synthase ⊖

Tubular Disorders

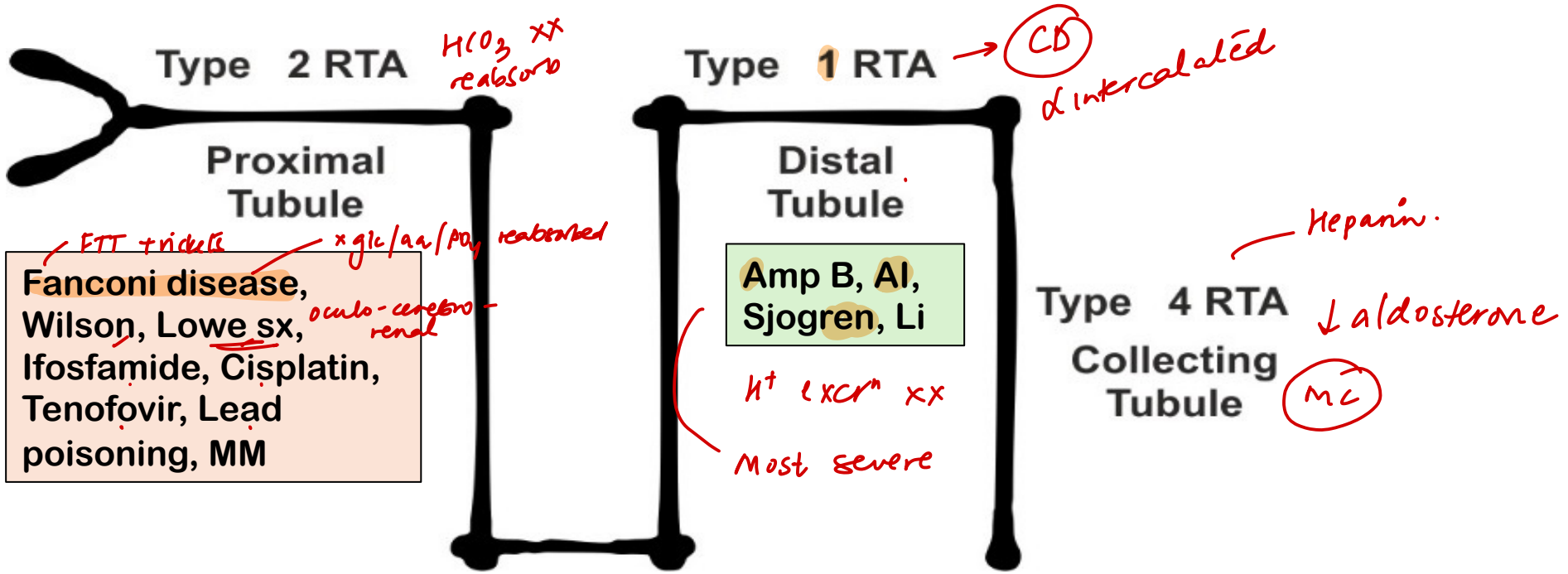


Dx	Bartter	Gitelmann	Gordon	Pseudohypoaldost	Liddle
BP	↓	↓	↑	↓	↑
K^+	↓	↓	↑	↑	↓
P^H	alkalosis	alkalosis	acidosis	acidosis	alkalosis
Ca^{2+}	V_{Ca} ↑	V_{Ca} ↓ S_{Ca} ↑	–	–	–

SNHL
type IV
poly H
S. Mg ↓ *

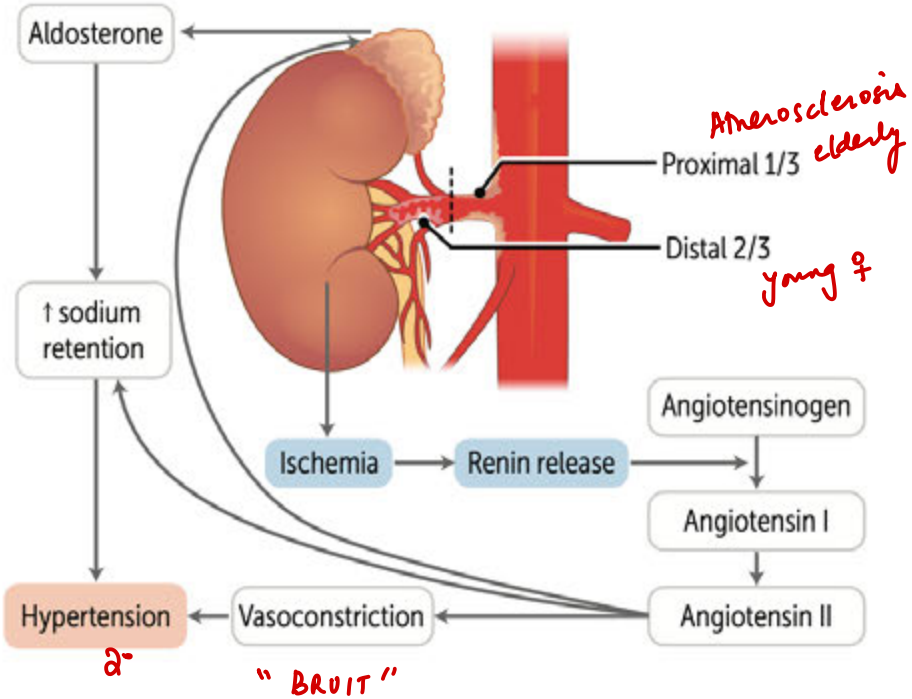
	K^+	acid-base
Acidazolide	↓	metab acidosis
Loop / Thiazide	↓	alkalosis
SEAT	↑	acidosis

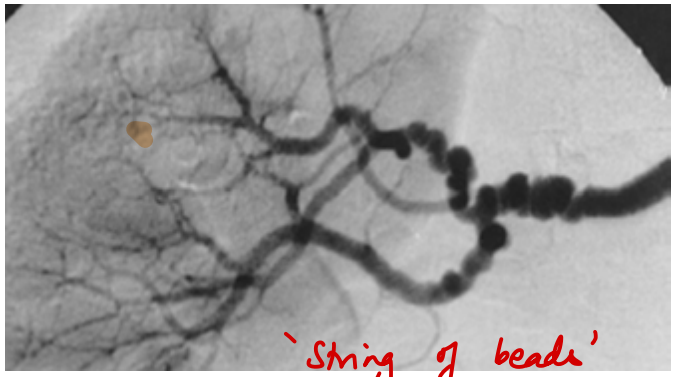
Renal Tubular Acidosis → Metab acidosis (NAGMA)



	K	Ca	Urinary pH	Nephrolithiasis
2	↓	↓	↓	–
1	↓	↑	>5.5	⊕⊕
4	↑	↓	↓	–

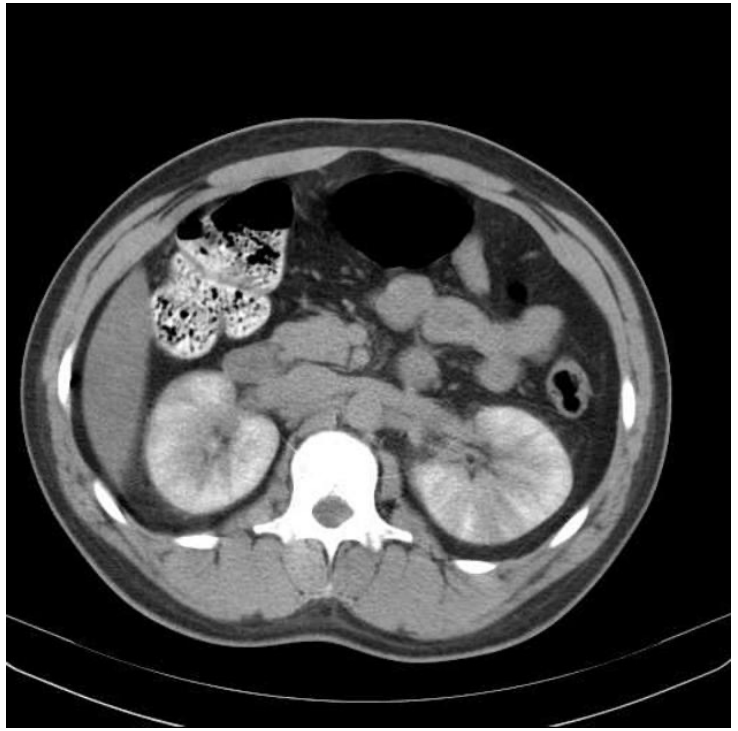
Reno-Vascular Diseases





`String of beads'

& FMD – Fibromuscular dysplasia

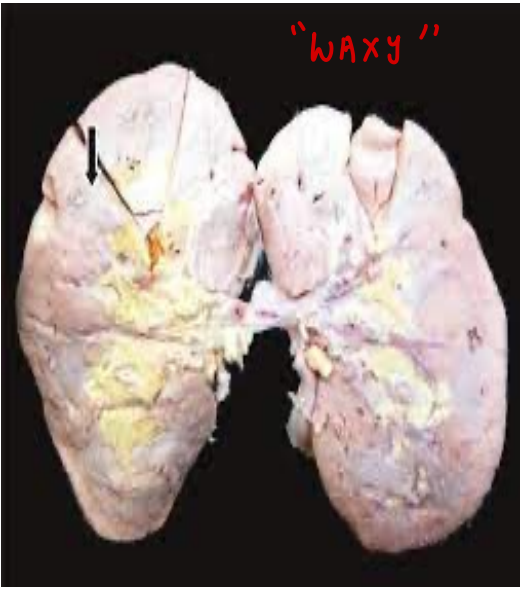


Renal - Segmental - Interlobar - Arcuate - Interlobular artery - Afferent arteriole - Glomerulus - Efferent arteriole - Peritubular capillaries

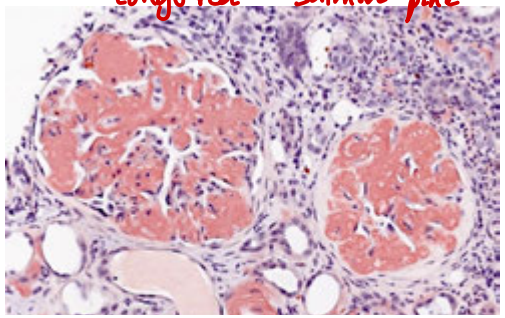
Acute ureteric obstruction/ pyelonephritis/ renal vein thrombosis

Striated nephrogram

Renal Pathology



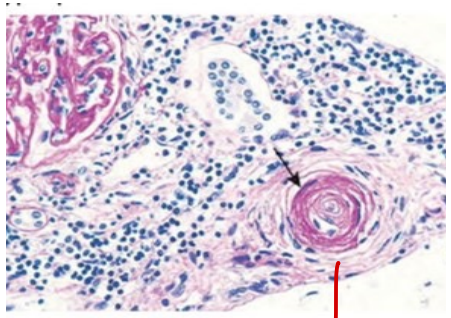
Congo red – salmon pink



Amyloidosis

mc organ: kidney

B/L enlarged → HIV, DM, B/L AD-PCKD

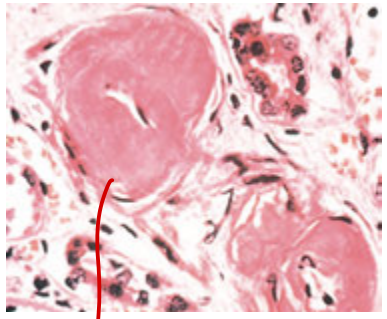


Flea bitten

Hyperplastic arteriosclerosis

↓

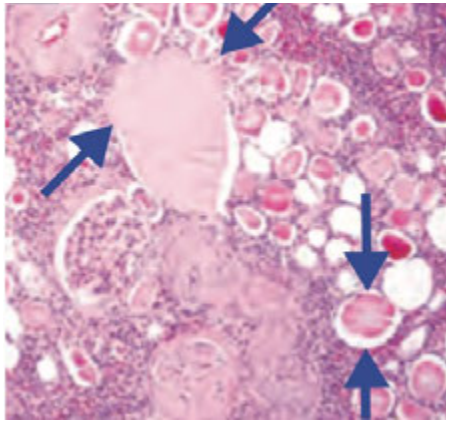
malignant hytn



Leather grey

Hyaline arteriosclerosis

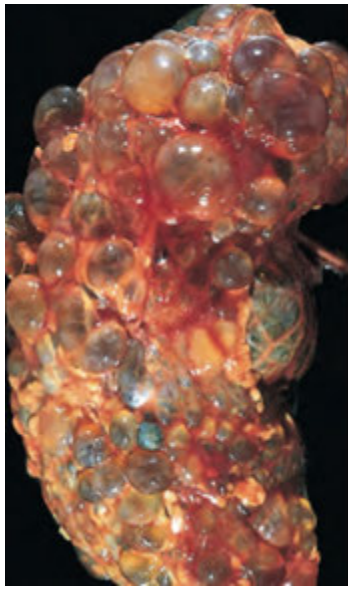
DM, Hytn



thyroidication of tubules

↓

chronic pyelo N



AD-PCKD

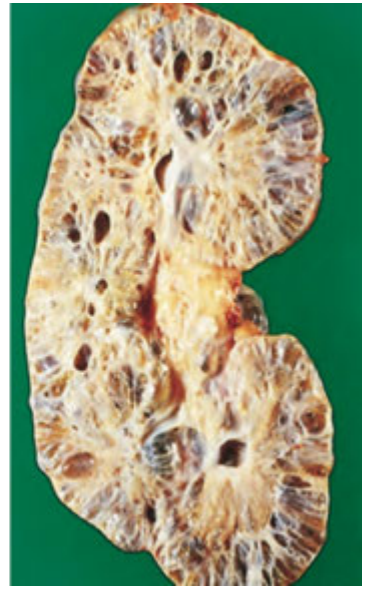
Chr 16,4: PKD1 & 2 Polycystin

mc: cysts - liver > pancreas > spleen

- Aortic dissection
- Berry aneurysm\
- Diverticulosis

- adults

↳ 50-60yrs.



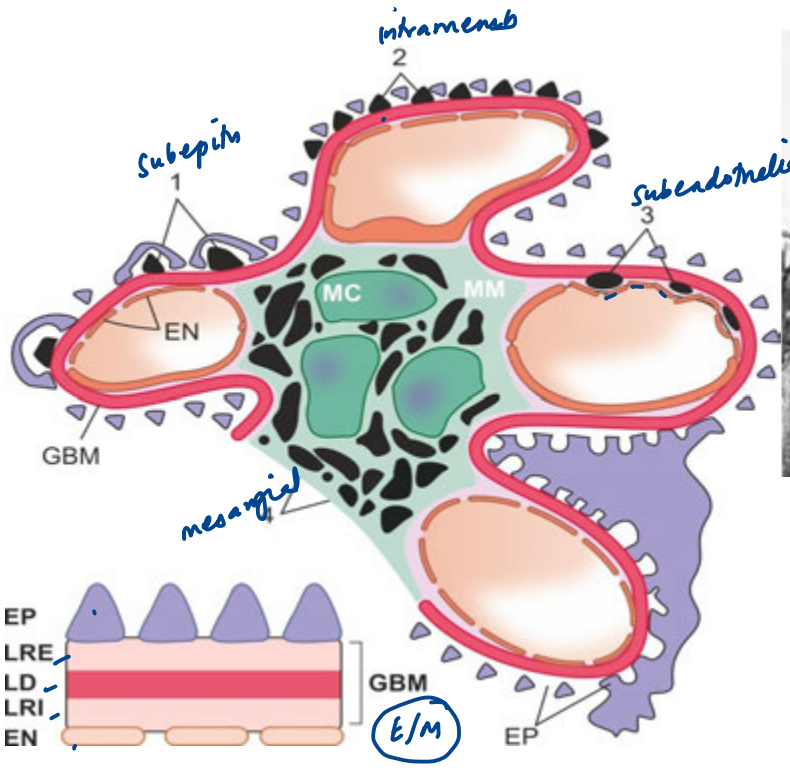
AR-PCKD

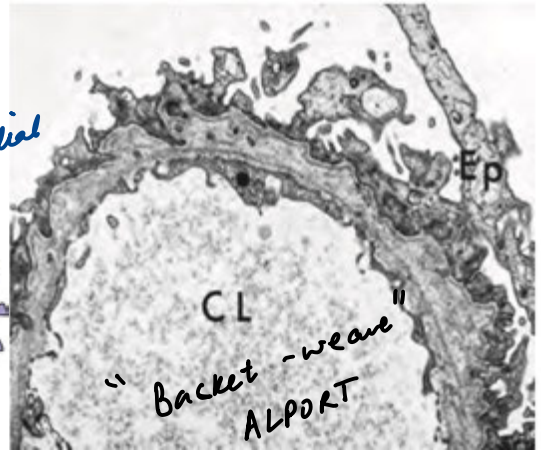
Chr 6: PKHD Fibrocystin

Congenital hepatic fibrosis

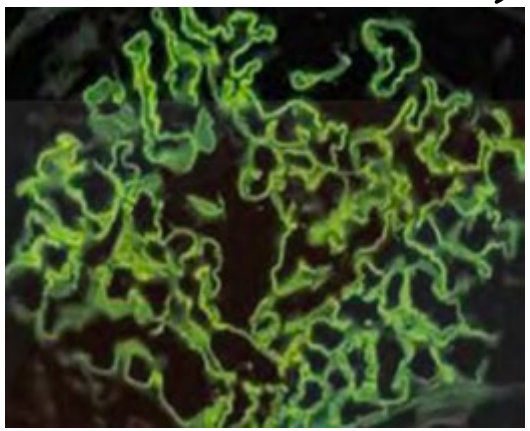
↳ 1yr.

Glomerular Diseases



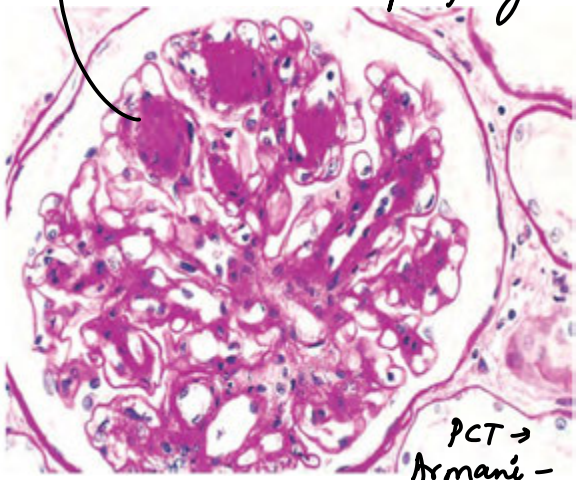


Linear IF (DIF)

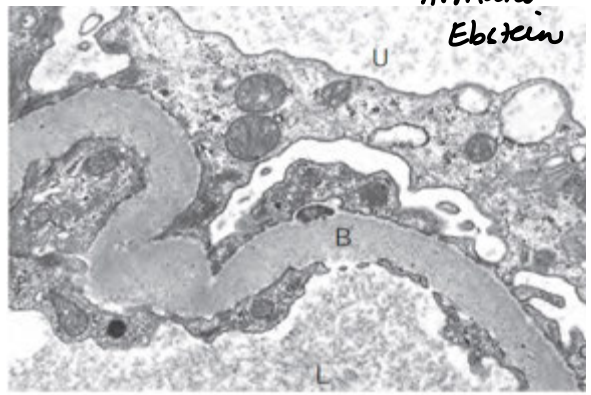


Diabetic nephropathy

K-W nodules (Kimmelsten-Wilson)



PCT → Armani-Ebstein



GBM thickening - earliest

- ↑ GFR
- albuminuria
  - 30-300 mg/dl
  - (+) dipstick
- ACR mg/g

TOC: ACEI / ARB (Telmisartan) PPAR γ (+)

TYPE IV COLLAGEN

α3 α4 α5

Goodpasture
anti-GBM
hematuria
hemoptysis
Ab / Linear IF

Thin BM D= Familial benign Hematuria

ALPORT
Ant lenticonus
SNHL
Hematuria

1- Sub-epithelial
- hump - PSGN
- spike & dome - membranous

2- membranous - MPGN type II

3- Subendothelial
- MPGN type I
- SLE

4- mesangial - IgA nephritis

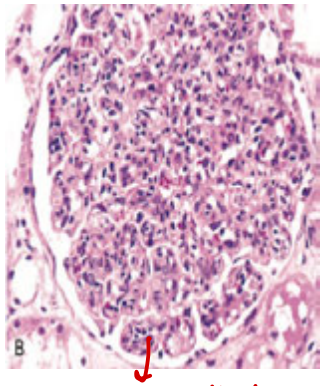
Nephritic Syndrome

Hematuria, Oliguria, Hypertension

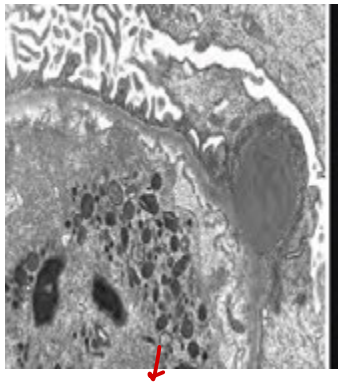
Buerger = TAO

PSGN

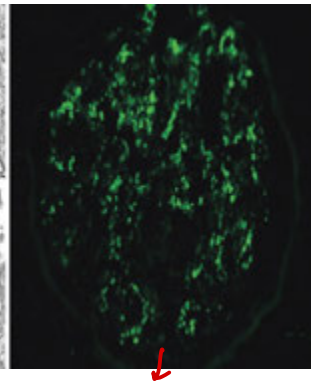
Child (mc)
Hematuria 10-21d after pharyngitis/impetigo (strain 12,4,1)
Type III hysn
C3 transient low (↓↓ persistent → RPGN)
70% Anti-DNase+
30% ASLO +



Hypercellular (↑↑ inflamm cells)



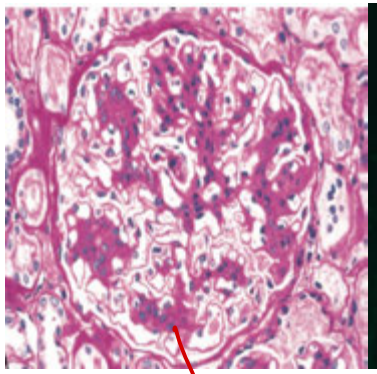
Subepithelial humps



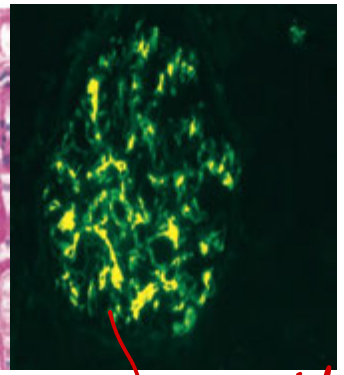
Granular IF

IgA Nephritis = BERGER Disease

Adult ("Syn")
Hematuria 3d after pharyngitis
Recurrent gross hematuria
C3 normal

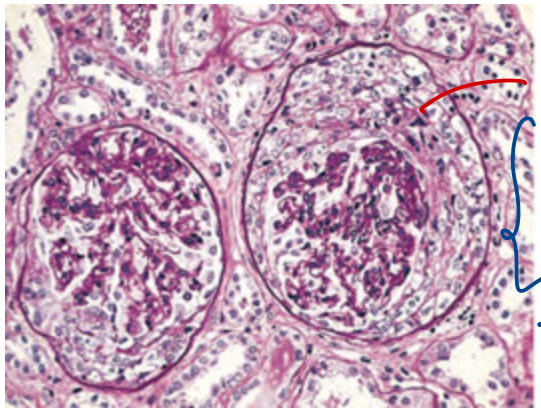


mesangial prolifer



mesangial deposits IgA.

Rapid progressive = RPGN



Crescents
- WBC
- Fibrin
- parietal epith cells
+ visceral epith cells

Linear: Goodpasture
Granular: PSGN
Pauci-immune: ANCA-mediated

- MPA (p-ANCA)
- WG (c-ANCA)

IgA Nephritis

Sparsentan: ARB + Endothelin -

Nephrotic Syndrome

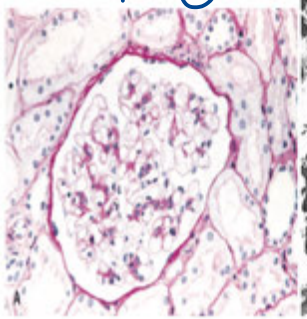
Proteinuria >3.5g/d, Edema, frothy urine / Lipiduria

1st – periorbital edema

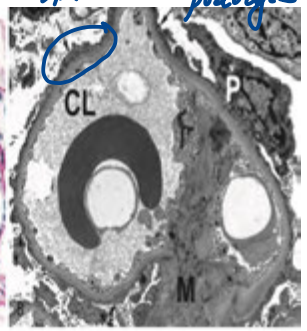
MINIMAL CHANGE DISEASE

Child → MC
Prior URTI
NSAIDS, Hodgkin's lymphoma
Urine loss of: selective albuminuria
- Ig ↓ → ↑ infxn
- Anti-thrombin ↓ → ↑ coag / RVT
- Lipoprotein ↓ → Hyperlipidemia

L/M (N)



E/M: effacement of podocytes



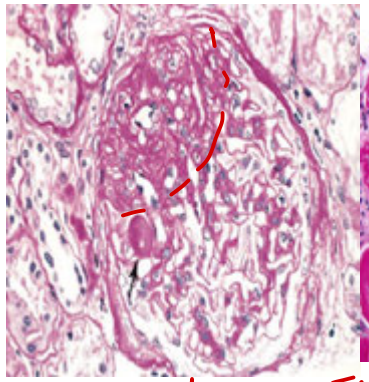
TOC: Prednisolone 2mg/kg x 6wks – taper x 6wks
SRNS: x response in 4–6 wks
DOC: TACROLIMUS
Steroid dependent NS: ≥2 relapses in 2wks of tapering
MMF / Cyclophosphamide / Levamisole – mild
FRNS: ≥2 – 6mon (severe) / ≥4 – 1yr (>8yr)

FSGS

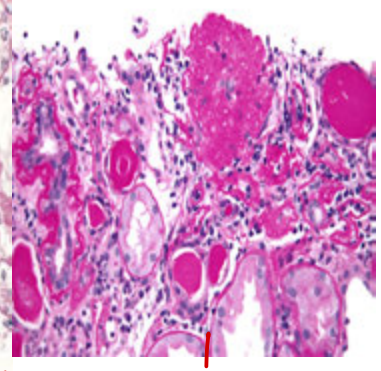
Adults – MC
Heroin
HIVAN: APOL1 polymorphism
Reflux nephropathy
Obesity
Sickle cell anemia
NPHS2: Podocin-AR FSGS
Actinin 4: AD FSGS
TRPC6: Adult FSGS

Steroid resistant

(Fibrinogen ↑)



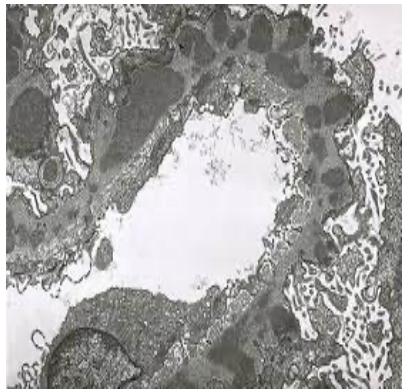
focal / segmental



Collapsing variant
- HIV
- COVID-19
- Bisphosphonates

Membranous

MC in elderly
Adenoca / melanoma
NSAID, penicillamine, gold
Hep B / malaria
PLAR2
Thrombospondin, CD10

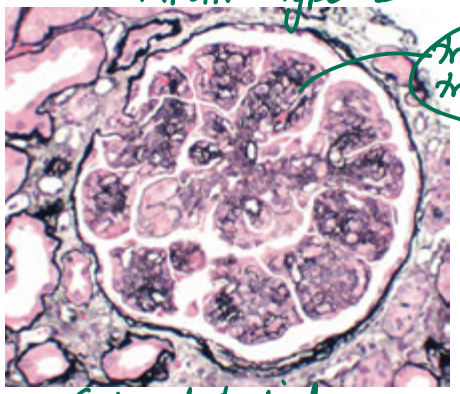


Subepithelial
"spike & dome"

MPGN

Adult
HCV / malaria
Cryoglobulinemia

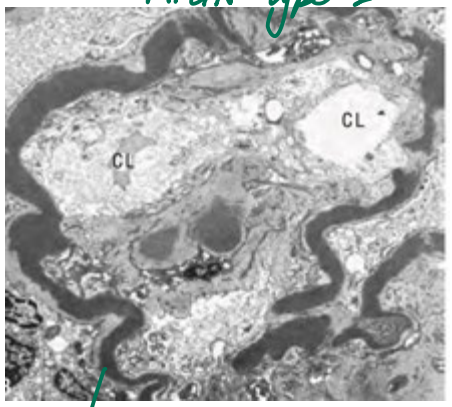
MPGN – type 1



tram-track

Subendothelial

MPGN type 2



membranous deposits
"dense"

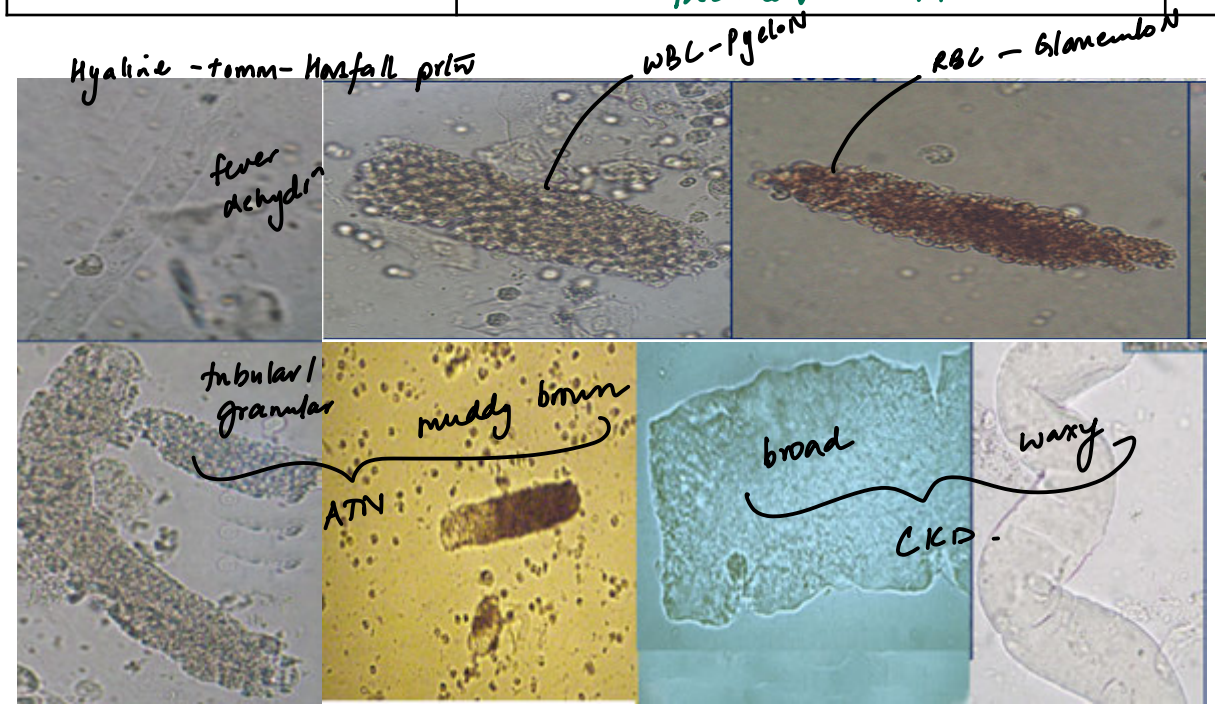
C3 NEF
C3

Nephrin NPHS1-Finnish type: Congenital NS

AKI vs CKD

	AKI	CKD
CMD	Maintained	LOST
Size	↑ / (N)	contracted
Urine Osmolarity	-	1.010 – isosthenuria
Anemia	–	++ EPO ↓↓
MBD	–	++ 1α OH ↓↓
Casts	tubular – ATN	broad / waxy

Sp. gravity
Best marker of tubular fx



Biomarkers of AKI:

- Cystatin C
- KIM-1
- NGAL
- TIMP2
- NABG

Renal papillary necrosis:

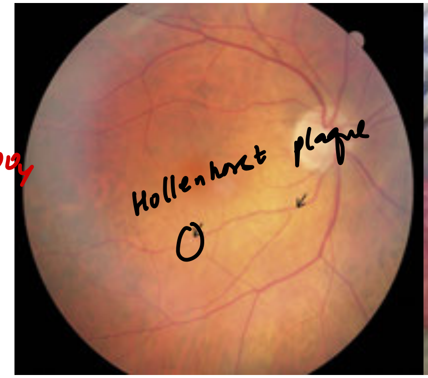
- NSAIDS
- Sickle cell disease or trait
- Acute pyelonephritis
- Infections (TB)
- Diabetes mellitus

Hematuria:
Glomerular: RBC casts, dysmorphic RBC, proteinuria

Non-Glomerular: isomorphic RBC / crystals

AKI

-	Pre renal	Acute Tubular necrosis
Cause	Hypovolemia, CHF, NSAID, ACE- ↓GFR	Sepsis, Ischemia, Nephrotoxins: Rhabdomyolysis, IVH, Tumor lysis, MM, Drugs, Iodinated contrast
FeNa $= \frac{C_{Na}}{C_{cr}} = \frac{U_{Na}}{P_{Na}} \times \frac{P_{cr}}{U_{cr}}$	<1%	>1%
Urine Na	<10 meq/L	>20 meq/L
Urine Osmolality	>500	<350
BUN/Creatinine	>20:1	<10:1
Urine casts	–	(+)(+)



Eosinophilia + Low complement
Atheroembolic D

Fever + Rash + Eosinophilia + Drugs
AIN (WBC casts)
β-lactams, Rifampicin, Allopurinol, AEDs, Diuretics

Vancomycin, Aminoglycosides, Tenofovir, Cisplatin, Cidofovir, Foscarnet, AmpB, Crystals: Acyclovir, Indinavir

h/o PCI < CIN – 48hr of contrast; atheroembolic D

Acute Kidney Injury – Phases
Initiation (damage)
Maintenance (oligo/anuric) < p. edema; ↑K+ / acidosis
Resolution: polyuria → risk of ↓K+ / alkalosis / ↓PO4

Risk KDIGO Stage 1	EGFR Decrease by 25%/ Creatinine Increase by 1.5x	UO <0.5 mL/kg/hour for 6 hours
Injury KDIGO Stage 2	EGFR Decrease by 50%/ Creatinine Increase by 2x	UO <0.5 mL/kg/hour for 12 hours
Failure KDIGO Stage 3	EGFR Decrease by 75% Creatinine Increase by 3x	UO <0.3 mL/kg/hour for 24 hours or anuric for 12 hour
Loss	Persistent renal failure > 4 weeks	-
End stage = CKD	Persistent renal failure >3 months	-

CKD

MCC of CKD: Diabetic nephropathy (↑ accelerated atherosc)
MCC of death: ♡ arrest
Anemia: EPO deficiency
Indication: Hb <10 g/dl — EPO ⊕ Darbapoeitin α (ensure that Fe stores adequate (Fe → EPO))
Target: 10 - 11.5 g/dL (↑ rbc mytn)
Bone disease: 1α OH ↓ vit D ↓ – Ca ↓ → 2° Hyper PTH (Renal osteo D); PO_4 ↑ (PTH ↑, ALP ↑)
Rx: vit D supplements + (P) binders
- Dapruductat HIF ⊖ → EPO ↑

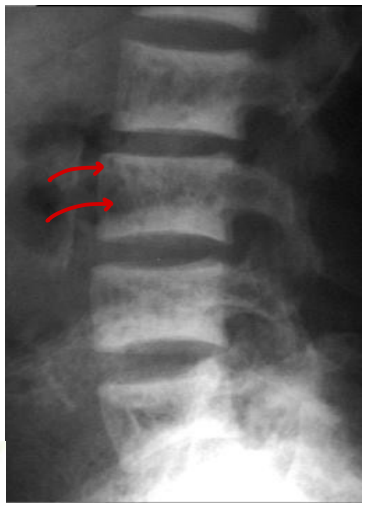
Calciphylaxis: Ca - PO_4 – arteriopathy
Acid-base: NAGMA → HAGMA
Uremia:
Pericarditis
P.Edema
pH <7.2
Potassium >6.5
Encephalopathy
Bleeding: plt dysfn

} dialysis

Dialysis disequilibrium syndrome DOC:
Mannitol

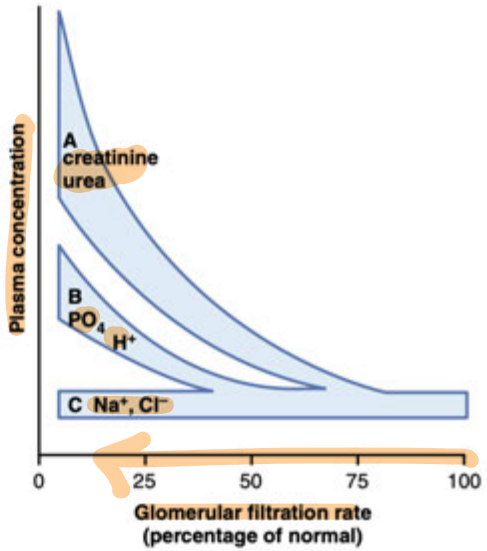
Stage of CKD	eGFR
Stage 1	≥ 90
Stage 2	60–89
Stage 3a	45–59
Stage 3b	30–44
Stage 4	15–29
Stage 5	<15 – RRT

↓ complications
Rx complications
prep for RRT



Rugger-Jersey spine

Uremic FROST



Acid-Base Balance

pH - 7.40
CO_2 - 40 mm Hg
HCO_3^- - 24 meq/L
Derived value in ABG: HCO_3

	Causes	pH	Primary Change	Compensation
METABOLIC ACIDOSIS	HAGMA NAGMA	↓	HCO_3 ↓	CO_2 ↓
METABOLIC ALKALOSIS	Hyperaldosteronism, Vomiting, Loop/thiazides Bartter-Gittleman	↑	HCO_3 ↑ 1 meq/L	CO_2 ↑ 0.7 mm Hg
RESPIRATORY ACIDOSIS	Hypoventilation Airway obstruction	↓	CO_2 ↑ 10mm↑	HCO_3 ↑ A - 1. C - 4.
RESPIRATORY ALKALOSIS	Hyperventilation (preg, PE)	↑	CO_2 ↓ 10mm↓	HCO_3 ↓ A - 2 C - 5

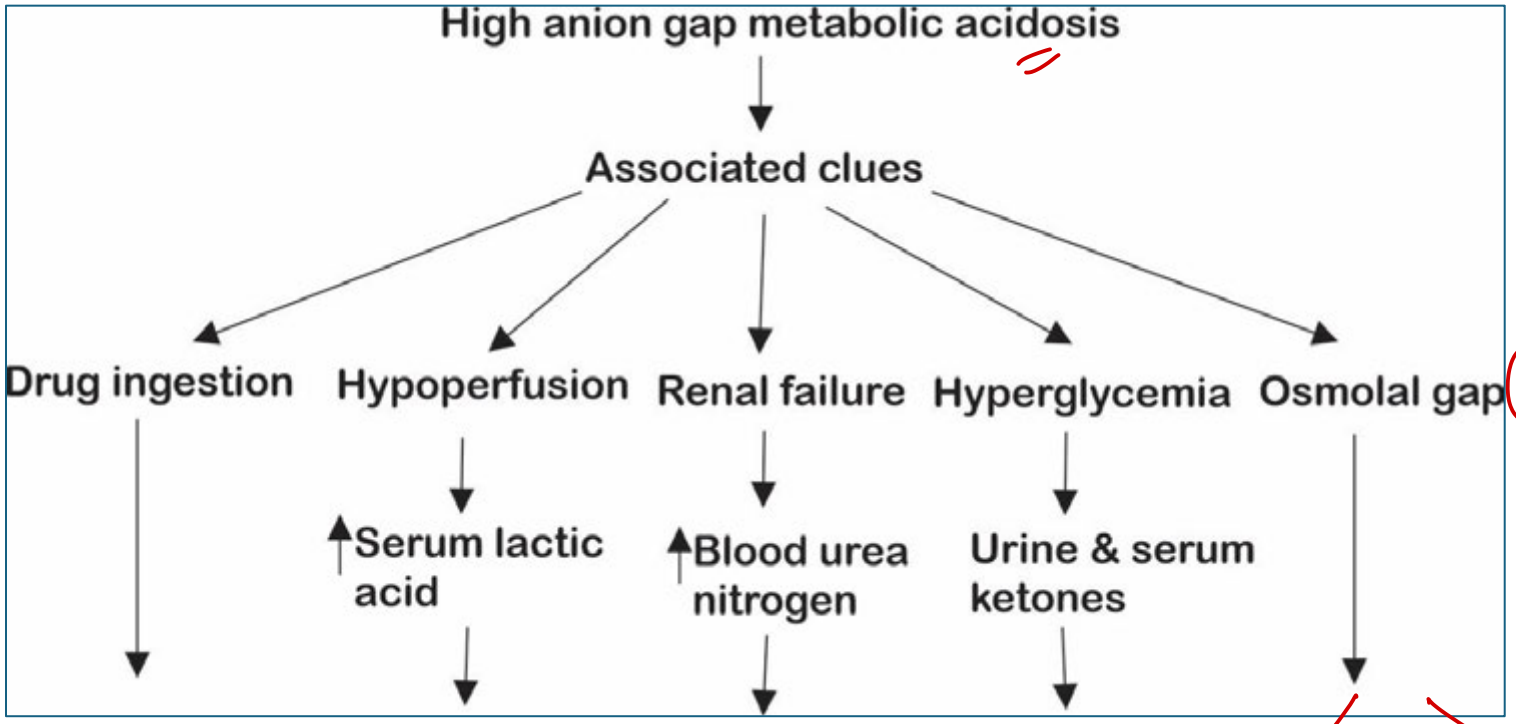
QR — Winter's formula

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

DKA - Kussmaul (↑ventln)

Metabolic Acidosis

Anion gap= (Na) - (HCO3 + Cl)
Normal: 8-12



- Salicylates (resp alkalosis → HAGMA)
- Lactic acidosis
- Uremia
- DKA
- ethylene glycol → Ca-oxalate urine
- methanol "Hooch tragedy" → blindness

Rx - Fomepizol

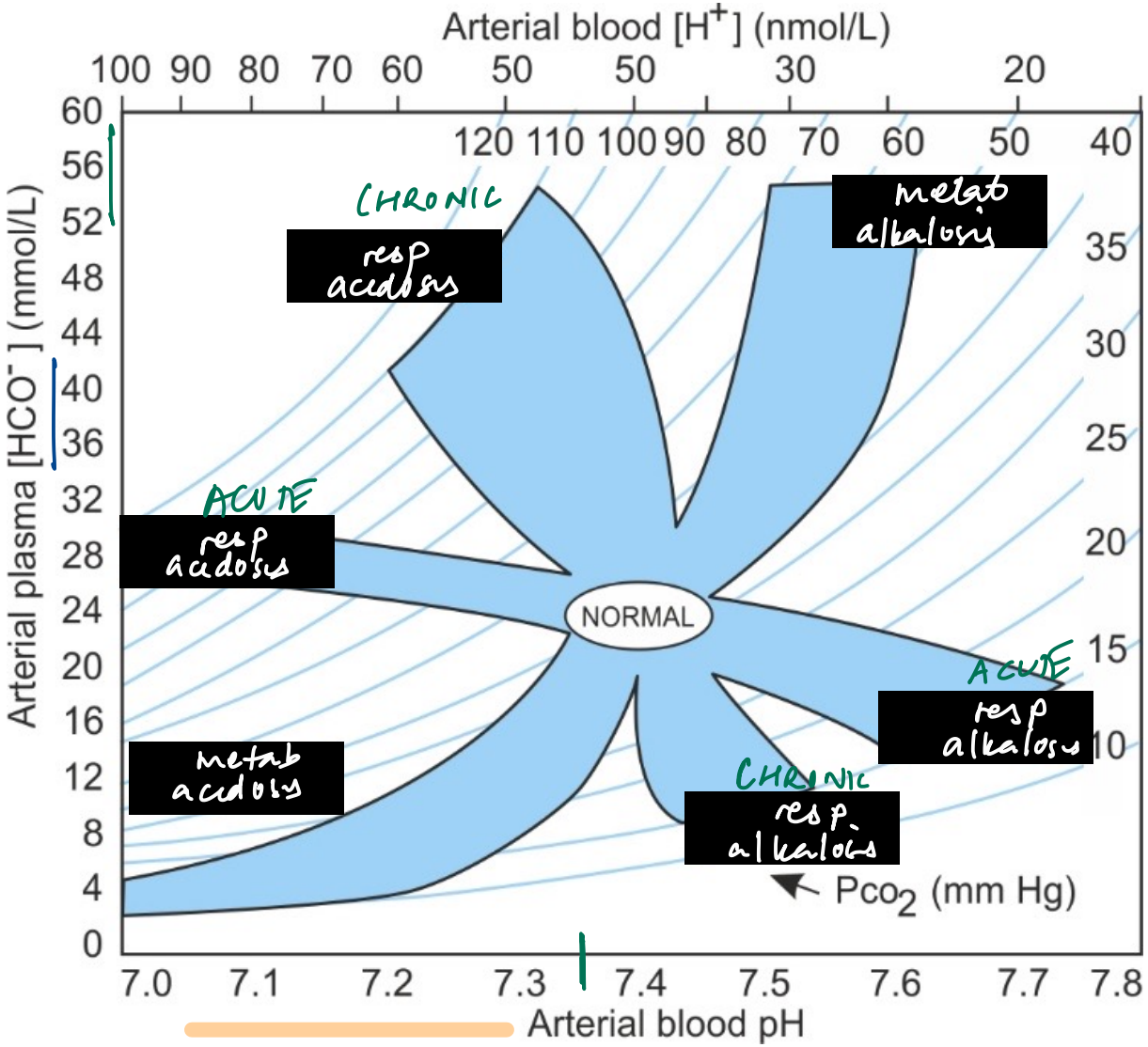
OR

NAGMA= Hyperchloremic acidosis:

- **Renal tubular acidosis** (V_{AG}: +ve = $V_{Na+K} - V_{Cl}$)
- **Diarrhea** (HCO_3 loss)
- **Addison disease/Spironolactone** - type IV
- **Carbonic anhydrase inhibitors** - type II
- **Hyperalimentation** TPN
- **Saline infusion** OR (NS)
- **Ureteral diversion** (e.g., ileal loop)

↑ ideal - vomiting

VS RL : HCO_3 (Liver) → metab alkalosis
→ diarrhea ideal.
→ CI. liver D


Arterial blood [H+] (nmol/L)
100 90 80 70 60 50 50 30 20
120 110 100 90 80 70 60 50 40
Arterial plasma [HCO-] (mmol/L)
60 56 52 48 44 40 36 32 28 24 20 16 12 8 4 0
35 30 25 20 15 10
CHRONIC
resp acidosis
metab alkalosis
ACUTE
resp acidosis
NORMAL
ACUTE
resp alkalosis
metab acidosis
CHRONIC
resp. alkalosis
Pco2 (mm Hg)
7.0 7.1 7.2 7.3 7.4 7.5 7.6 7.7 7.8
Arterial blood pH

On laboratory investigations in a patient, pH=7.3, pCO2=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, HCO3-28 and PCO2-50 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

36mm

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 $CO_2 = 36$

C. Metabolic acidosis with respiratory alkalosis

D. Respiratory alkalosis with renal compensation

Winter's :

$(1.5 \times HCO_3) + 8 \pm 2$

$(1.5 \times 14) + 8 \pm 2$

$21 + 8 \pm 2$

$= 29 \pm 2$

A patient who is a known case of CKD has complaints of vomiting. His ABG reports are as follows: pH-7.40, pCO_2- 40, HCO_3-25. Na-145, chloride-100. What is the metabolic abnormality?

AG : 145 − (100 + 25)

= 20

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

Electrolyte abnormalities

280-290 270 180/18 = 10 28/2.8 = 10

Serum osmolarity: 2(Na) + glucose/18 + BUN/2.8

MANAGEMENT of HypoNa

Sodium deficit: = TBW × (140 − Na$^+$)

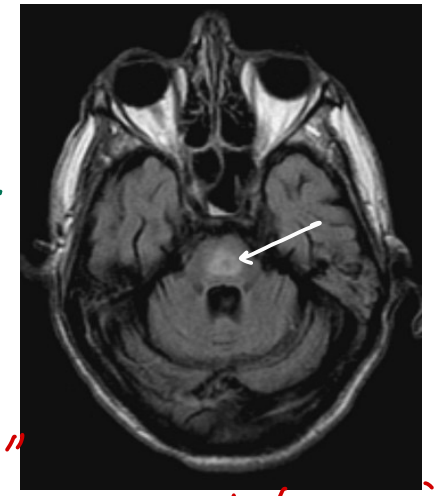
50kg ⇒ Na: 120 → 60/100 × 50 × 20 = 600 meq.

Max: 8 meq/l in a day

Severe-Seizures/coma: 3% Hypertonic

Overcorrection: CPM / ODS – pons

"locked in"



trident / snout sign

Drugs causing HyperK

- K sparing diuretics (SEAT)
- ACE-/ARB
- Digoxin (Na-K ATP)
- β-blocker
- Calcineurin inhibitors
- Pentamidine
- NSAIDs
- Heparin (type IV)
- Succinylcholine (cell lysis)
- Trimethoprim

(N) Na: 135-145 meq/L

(K): 3.5-5

Ca^{2+}: 8.5-10 mg/dl

transcellular spread ↓ ← insulin, β agonist, alkalosis

Hyper Na$^+$

Free water deficit: $\frac{Na - 140}{140} \times TBW$

60% ⇒ ♂

50% ⇒ ♀

Management of Hyperkalemia: QQ

1st step: 10% Ca gluconate (♡ stabilise)

~~QQ~~

Transcellular spread: ← insulin + glc; β agonist (salbutamol, epi N); $NaHCO_3$ (alkalosis)

Eliminate: Diuretics – loop

Most effective: Hemodialysis

Binders:

- Sodium polystyrene sulfonate (SPS / Kayexalate)
- Patiromer
- Sodium zirconium cyclosilicate – selective