18 CHAPTER

INTEGRATED RENAL

Renal Physiology

- Clearance is the **amount of blood** that is cleared of a certain substance in unit time.

$$\frac{\text{Conc in } \textbf{urine}}{\text{Conc in } \textbf{plasma}} \times \textbf{Rate of urine (ml/min)}$$

- Clearance **>** GFR **: PAH** *(secreted)*
- Clearance **=** GFR **: Inulin** *(passes unchanged)*
- Clearance **<** GFR **: Glucose/Sodium/bicarbonate** *(absorbed)*

Clearance of **Inulin** is a proxy for **GFR**
Clearance of **PAH** is a proxy for **RPF** (renal plasma flow)

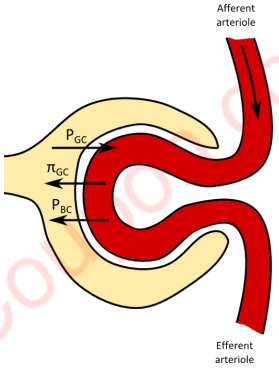
Counter Current

Multiplier
Loop of henle
(establishes the counter current)

Exchanger
Vasa recta
(maintains it)

Regulation of glomerular blood fllow

1. **Afferent arteriolar constriction** : Reduces RPF and GFR
2. **"Severe" efferent arteriolar constriction** : Reduces RPF and GFR
3. **"Moderate" efferent arteriolar constriction** : Reduces RPF but *increases GFR* ***(filtration fraction increased)***
4. **High plasma protein** : GFR decreases and RPF same ***(filtration fraction decreased)***
5. **Low plasma protein** : GFR increases and RPF same ***(filtration fraction increased)***
6. **Ureter constriction :** GFR decreases and RPF same ***(filtration fraction decreased)***



- **Prostaglandins** dilate afferent arteriole
- Hence, **NSAIDs** cause constriction (Reduce GFR)

Prostaglandins Dilate Afferent arteriole (PDA)
Angiotensin Constricts Efferent arteriole (ACE)

- **Angiotensin** constricts efferent arteriole
- **ACE inhibitors/ARBs** hence dilate it and reduce GFR

In Shock

- Both afferent and efferent are constricted : **Low RPF and Low GFR**
- Filtration fraction is **increased**

Myogenic Autoregulation

- Increased **stretch** of arteriole causes calcium entry
- **Calcium** causes vasoconstriction
- Protects kidney in hypertension

JG Apparatus

Macula Densa
Densa DCT

Tubuloglomerular feedback

- Chemoreceptors
- Between **DCT** and **thick ascending loop** of LOH

Increased sodium
- Adenosine released
- Aff. arteriole constriction (GFR decreased)

Decreased sodium
- Prostaglandins released
- Aff arteriole vasodilation (GFR increased)

JG cells
Around Glomerulus : Afferent arteriole

Baro-receptor

- Modified smooth muscle cells of **afferent arteriole**
- Activates **RAAS** if GFR low

Lacis cells
- Mesangial cells
- Anti inflammatory

Renal Tubules

Proximal Convulated Tubule

SGLT²

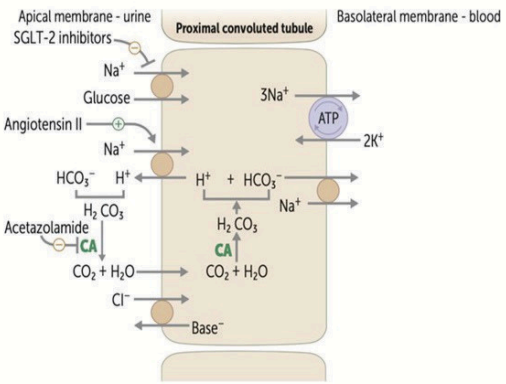
- **100 % glucose** absorption, **70% of NaCl** absorption in PCT
- Secondary active transport
- Inhibitors used for treatment of diabetes (dapaglifozin)

Na - H antiport

- H+ pushed into lumen : traps **HCO³** and **NH³**
- Essential for **HCO³ absorption** and **ammonia excretion**.
- **Angiotensin** is agonist at this receptor

Carbonic anhydrase/ Type 2 RTA

- Blocked by **acetazolamide** ***"Acid"azolamide***
- HCO3- lost in urine : **RTA type 2**
- Ammonia can't be excreted
- Sodium not absorbed (absorption in distal part : *Hypokalemia*)



Other causes of Type 2 RTA

- Wilson's disease
- Fanconi's disease (Global PCT dysfunction)

Thin Descending Limb of LOH

- Only permeable to water
- **Aquaporin 1** present

Thick Ascending Limb of LOH

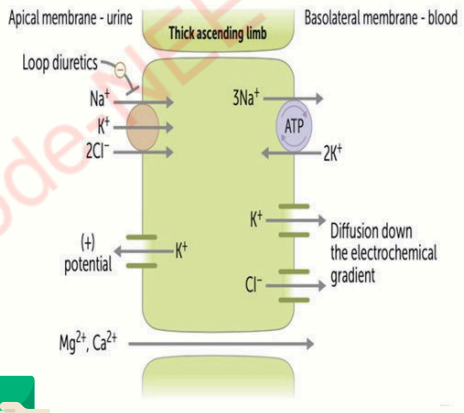
Impermeable to water (urine dilutes)

Na+ K+ 2Cl-

- Absorption of **Na**(25%), **K**, **Cl**
- Causes increased K+ on membrane : forces paracellular absorption of **Mg²** and **Ca²**
- Inhibited by **Loop diuretics** and in **Barter syndrome**

Loop diuretics

- High ceiling diuretics, used in **Pulmonary edema**
- Loss of **calcium** in urine ***(loops lose Calcium)*** : urinary stones
- Na+ reabsorption in distal tubes (*hypokalemia* and *alkalosis*)
- **Ototoxic**
- **Sulfa allergy**
- Can precipitate **Gout**



"Barter in loop"

Distal Convulated Tubule

Na Cl cotransporter

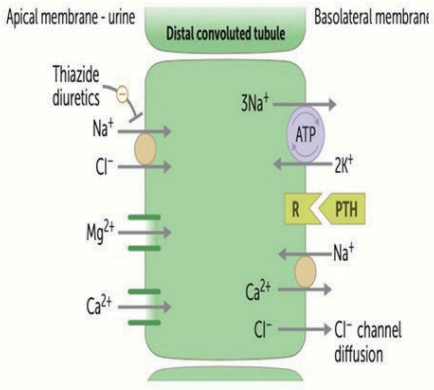
- NaCl absorption
- Blocked by **Thiazide diuretics** and in **Gittleman Syndrome**

Thiazide diuretics

- Increase **calcium** absorption (*preferred in osteoporosis*)
- First line for **CHF, Hypertension, Calcium stones**
- **Sulfa** allergy
- Citrate combines with calcium, in absence of calcium there is too much oxalate in urine which **precipitate stones**.
- Na+ reabsorption in distal tubes (*hypokalemia* and *alkalosis*)

H+ ATPase / Type 1 RTA

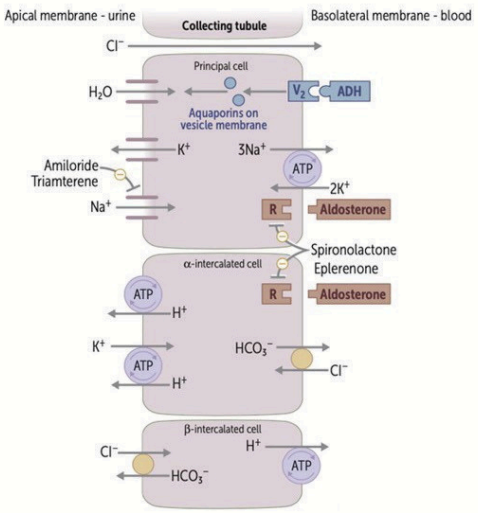
- **H+ ATPase** pushes H+ into lumen
- If this H+ ATPase is blocked, it causes **type 1 RTA**
- **Increased pH** of urine (alkaline urine)
- Can cause **urinary stones** (***one : stone***)
- Associated with autoimmune conditions (**SLE, Sjogrens, Type 1 DM**)



PTH receptor

- PTH acts in DCT
- ↑ Calcium absorption and
- ↓ Phosphate absorption

Collecting Duct



Na Cl cotransporter

- NaCl absorption
- Blocked by **Thiazide diuretics** and in **Gittleman Syndrome**

"Gillete for thigh"

Thiazide diuretics

- Increase **calcium** absorption (*preferred in osteoporosis*)
- First line for **CHF, Hypertension, Calcium stones**
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Vasopressin (ADH)

- Acts on **V^2 receptors** (*V^1 receptors in vascular smooth muscles*)
- **Principal cells** of CT
- Aquaporins expressed
- *Free water absorption*
- *Conditions associated with ADH*

SIADH

- **Excess** ADH secreted
- Low serum sodium but increased urinary sodium
- **Euvolemic hyponatremia**
- Causes : **Small cell ca. of lungs**, meningitis, CNS surgeries
- Treatment : **VAPTANS**

Diabetes Insipidus

- **Insufficient** ADH
- Large amounts of urine
- **Hypovolemic hyponatremia**
- Treatment: **Desmopressin**

K+ sparing diuretics *(SEAT)*

S	Spironolactone	Blocks ***Na+ channels***
E	Eplerenone	
A	Amiloride	Blocks ***aldosterone***
T	Triamterene	

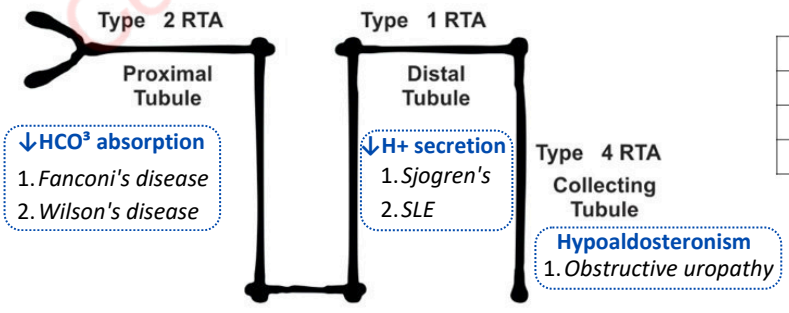
Aldosterone / Type 4 RTA

- Receptor present in **intercalated cells** *(vowels stick)*
- Express : **ENaC** and **ROMK** channels
- This causes **Na+ absorption** and **K+ excretion**
- **H+** is also excreted in exchange of Na+
- *Gain of function* of ENaC : ***Liddle's syndrome***
- **Hypo-aldosteronism** causes **Type 4 RTA** *(mc RTA)*

"Little ENaC"

Renal Tubular Acidosis

Metabolic acidosis due to *problem in renal tubules*



2 - 1 -4
Low low More

	serum K+	serum Ca++	Urine pH	Nephrolithiasis
Type 2	↓	↓	↓	↓
Type 1	↓	↑	↑	↑
Type 4	↑	↓	↓	↓

*All **high** for **1***
*All **low for rest***

Nephritic Syndromes

Inflammation** present, hence Nephr**itic

- **Cola** colred urine /dysmorphic **RBCs**/ RBC Casts
- Hematuria / oliguria / hypertension

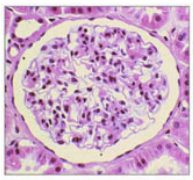
Pharyngitis

Child

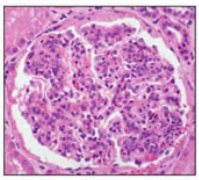
10-21 days after pharyngitis

PSGN

- **Glomerular** proliferation
- Sub-epithelial **humps**
- **C3** and **IgG** on immunoflorescence



Normal glomeruli



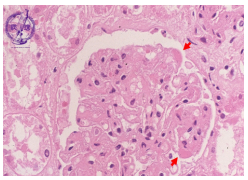
*Inflammed glomeruli with **neutrophils***

Adult

3 days after pharyngitis

Berger's Disease

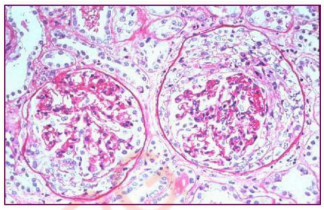
- **Mesangial** proliferation
- **IgA** in mesangium (aka IgA nephritis)
- **MCC** of nephritic syndrome



Mesangial proliferation

RPGN

- **Mesangial** proliferation
- Complication of **PSGN** (< 5%)
- It is usually **immune-mediated** (ANCAs, anti-GBM, ANA).
- Hence seen in Good Pasture syndrome and Wegner's.



Crescents are made up of

1. Proliferated epithelial cells
2. WBCs
3. Fibrin

Nephrotic Syndromes

- Proteinuria **>3g/day,** frothy urine
- Destruction of GBM
- **Maltese cross** in urine *(also seen in Fabry's disease)*

Nephrotic Syndrome

Child

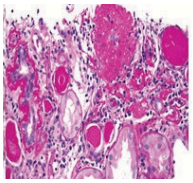
Minimal Change disease

- aka **Lipoid Nephrosis**
- *No changes* seen on light microscopy
- **Effacement of foot processes** on electron microscopy

Adult

FSGS

- **<50% of glomeruli** involved in parts
- **HIV** / SCA / Obesity
- **Collapsing variant** has *worst prognosis*
- **Glomerular tip variant** has *good prognosis.*



Collapsing Variant

MPGN

- **Thick GBM**
- **Hepatitis B/C**, malaria

Type 1

Tram track appearance

Type 2

Dense deposits

2 dense

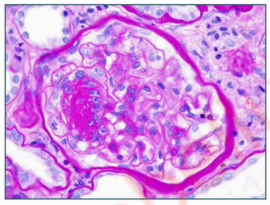
Elderly

Membranous Nephropathy

Elders have membranous skin

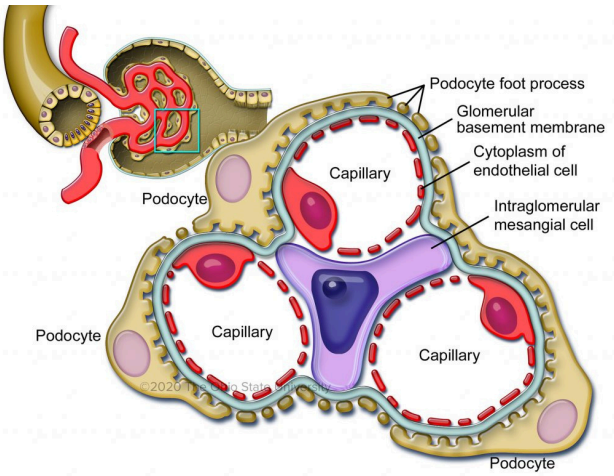
- Associated with **adenocarcinoma** (lung/colon) and **melanoma**.
- Antibodies against ***Phospolipase A2 receptors***
- *Sub epithelial* **Spike and Dome** on electron microscopy

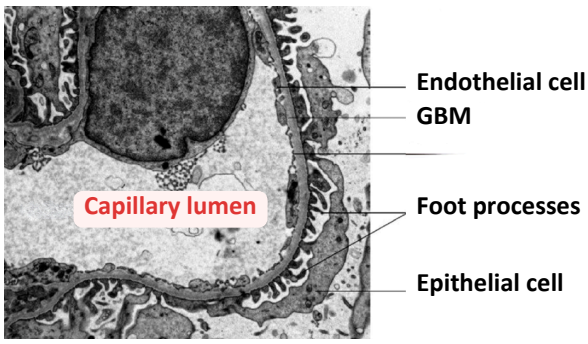
Nodular Glomerulo-sclerosis

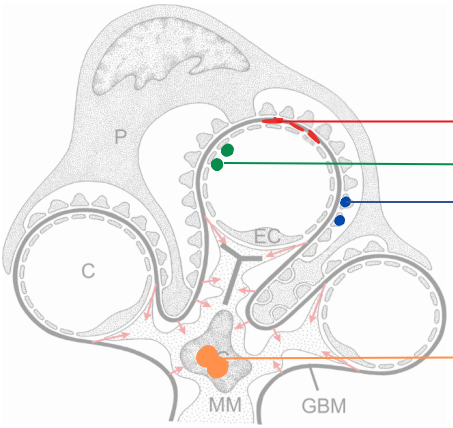


- aka **Kimmelsteil Wislon Disease**
- PAS (+)
- Seen in Diabetic nephropathy

Deposits on Electron Microscopy







Intra-membranous *MPGN type 2*

Sub-endothelial *MPGN type 1*

Sub-epithelial

- **Humps :** PSGN

- **Spike and domes :** Membranous

Mesangial *Berger's dis, RPGN*

Alport Syndrome

Basket weave pattern of basement membrane on EM

- **Type 4** collagen disorder (α5)
- **Family history** present
- T/t : **Ace inhibitors**
- Definite management is **transplantation** (doesn't recur)

Anterior lenticonus

Can't see
can't pee
can't hear a
buzzing bee

Hematuria M/c presentation

SNHL

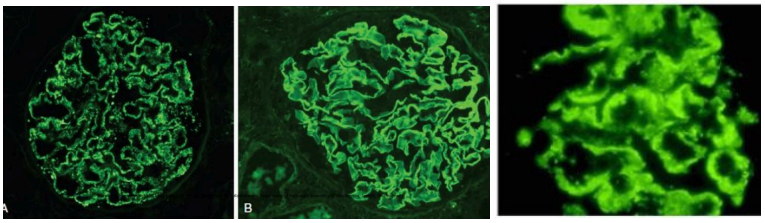
Type 4 collagen disorders

(α3)	(α4)	(α5)
Good Pasteur's Syndrome	**Thin BM disease** aka Benign familial hematuria	**Alport syndrome**

- **Anti GBM** antibodies
- Hematuria + Hemoptysis (*Pulmo-renal*)
- d/d : MPA, Wegner's, EGPA

Immunofluorescence

1. **Linear :** *Good Pasteur's syndrome (RPGN)*
2. **Granular IgG:** *PSGN* (kids), *Membranous* (Elderly)
3. **Granular IgA in mesangium :** *Berger's disease*
4. **Full house effect :** *Lupus Nephritis*



Granular **Linear** **Full House effect**

Renal Failure

Renal failure

AKI

- Size maintained

Pre renal
(No perfusion)

- **Sodium and urea aew reabsorbed** (tubules are normal)
- **FeNa < 1%**
- Urine **Na < 20**
- Urine **osmolality is high**
- Urea/creat is >20 (normal reabs. of urea)
- No casts

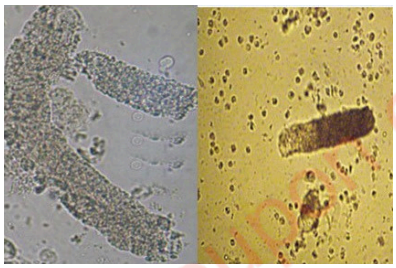
1. *Shock*
2. *Hepato-renal syndrome*

Renal
(Acute tubular necrosis)

- **Sodium and urea not reabsorbed** (tubules are impaired)
- **FeNa > 1%**
- Urine **Na > 20**
- Urine **osmolality is low** (no active secretion)
- Urea/creat is <10 (no reabs. of urea)
- **Granular/muddy brown casts**

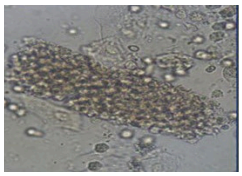
SIN
1. *Sepsis*
2. *Ischemia*
3. *Nephrotoxins*

AKI markers
- Kim **1**
- TIMP **2**
- Cystatin **C**
- NGAL
- IGFBP 7
- Osteopontin

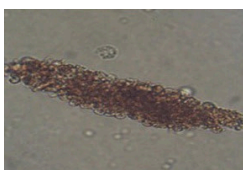


Granular/Muddy cast

Hyaline cast
- Seen normally in urine
- **Tam Horsfall** protein



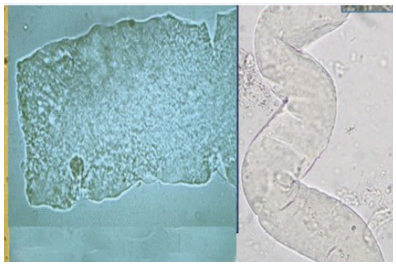
WBC cast
Pyelonephritis



RBC cast
Nephritic Syndrome

CKD

- **Contracted** kidney and *cortico medullary differentiation* lost
- **Isosthenuria** (constant urine osmolality of 0.010)
- **AOCD** (erythropoeitin def.)
- **Secondary hyperPTH** (renal osteodystrophy)
- **Waxy-broad** cast



Waxy broad cast

Conditions associated with CKD

1. **Low Vit D** synthesis : Low calcium and secondary hyper PTH
2. **AOCD**
3. **Hyperkalemia** (*K+ can't be excreted*)
4. **NAGMA** in early CKD (*HCO3 loss*)
5. **HAGMA** in late CKD (*can't excrete toxic substances*)
6. ***Water intoxication*** (*MCC of convulsions in CKD*)

Indications of dialysis

1. **Refractory acidosis**
2. **Refractory hyperkalemia**
3. ***BAL*** intoxication (Barbiturates, Alcohol, Lithium)
4. **Uremia** in ESRD (*when **GFR < 15***) presents with
   - *Asterexis*
   - *Pericarditis*
   - *Seizures*

Complications of dialysis

1. M/c complication : **Hypotension**
2. **Dialysis equilibrium syndrome** (removal of urea reduces blood osmolality, causing Cerebral edema), aka ***reverse urea effect***.
3. *Peritonitis* in peritoneal dialysis

Acid base imbalance

Normal values

1. pH : **7.4**
2. CO^2 : **40** *40 divisible by 2*
3. HCO^3 : **24** *24 divisible by 3*

"Compensation is always in same direction as primary change"
*eg. CO2 **increased** in resp. acidosis then HCO3 will **increase** as compensation*

Winter's formula

*For compensation in **metabolic acidosis***

$CO^2 = [\ \mathbf{1.5}\ (HCO^3) + \mathbf{8}\ ] \pm \mathbf{2}$

Anion gap= (Na + K) - (HCO3 + Cl)

Represents unmeasured anions

Check pH

- pH > **7.4** (**Alkalolsis**)
  - CO^2 < **40** (**Respiratory** Alkalolsis)
    - *Compensation* (**HCO^3** decreased)
  - HCO^3 > **24** (**Metabolic** Alkalolsis)
    - *Compensation* (**CO^2** increased)
- pH < **7.4** (**Acidosis**)
  - HCO^3 < **24** (**Metabolic** Acidosis)
    - *Compensation* (**CO^2** decreased)
    - **Check Anion Gap**
      - **12 ± 4** → **Normal anion gap met. acidosis (NAGMA)**
        - **HCO^3 is lost** causing acidosis
        - Anion gap maintained by **increase in chlorine**
        - Hence aka ***Hyperchloremic acidosis***
        - Check **Urine Anion Gap**
          - **High** urine anion gap
            - **Renal tubular acidosis**
          - **Normal** urine anion gap
            1. **Diarrhea**
            2. **Ureteric diversion**
      - **> 16** → **High anion gap met. acidosis (HAGMA)**

Unmeasured anions (acids) in blood

1. **Acidic drugs** : Salicylates (*aspirin*) or Isoniazid
2. **Lactic acidosis** : Sepsis
3. **Uric acidosis** : Renal failure
4. **Keto acidosis** : DKA
5. **Methanol** : Retinotoxic (*Hooch tragedy*)
6. **Ethylene glycol** : Ca. oxalate crystals in urine

Salicylates

- *Initially cause hyperventilation and **respiratory alkalosis***
- *Later cause **HAGMA***

On laboratory investigations in a patient, pH=7.3, pCO2=35 mm Hg, What is the likely acid base imbalance?

pH 7.3 : **Acidosis**
↓
Low $C0^2$: **Can't be resp. acidosis**
↓
Metabolic acidosis with *respiratory compensation*

A patient is having pH-7.12, HCO3-28 and PCO2-50 mm Hg. What is the acid base disorder in this patient?

pH 7.12 : **Acidosis**
↓
High HCO^3 : **can't be met acidosis**
↓
High pCO^2 : **resp acidosis**
↓
Resp acidosis with *metabolic compensation*

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?

Anion gap : (Na+K) - (CL+ HCO^3)

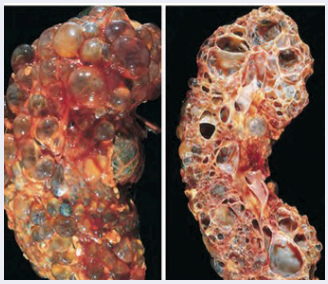
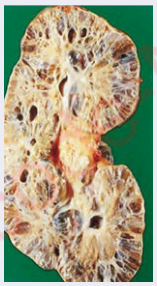
↓

145-125

↓

20 : **high anion gap, hence HAGMA**

Poly-cystic kidney disease

ADPKD	ARPDK
Most common	Most severe
Onset age >30	Infants and children
Half get ESRD by 60	Infant renal failure
Cerebral aneurysm	Liver fibrosis,death
 **Large cysts** (Rough outer contour)	 **Smaller cysts** (Smooth outer contour)

Cerebellum

Mission NEET PG 2.0 – 3rd Batch

Comprehensive Strategy to Ace

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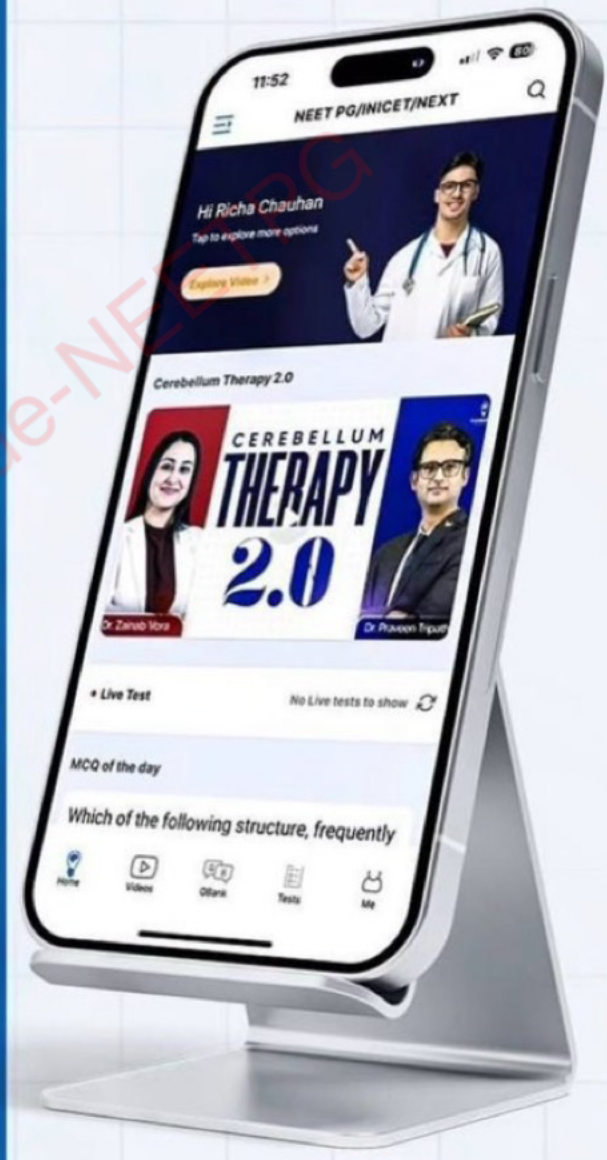
Tentative Schedule



Mission NEET PG/INI CET 2.0 - 3rd Batch

Topic	Date	E&D
Pharmacology (Dr. Gobind Rai Garg)	25th-29th Nov	
Pathology (Dr. Sparsh Gupta)	30th Nov-4th Dec	
Combined E&D (Pharma + Patho)		5th Dec
Medicine-I (Dr. Dilip Kumar)	6th Dec - 9th Dec	
10th - Dec - Break		
Medicine-2 (Dr. Dilip Kumar)	11th Dec - 14th Dec	15th Dec
Physiology (Dr. Pooja Nigade)	16th Dec - 19th Dec	20th Dec
BTR E&D (Integrated Subjects) (Dr. Zainab Vora)		21st Dec
Biochemistry (Dr. Ankur Jain)	22nd Dec - 25th Dec	
FMT (Dr. Atul Gupta)	26th-28th Dec	
Biochemistry & FMT Combined E&D		29th Dec

SWIPE LEFT

Topic	Date	E&D
BTR E&D (FMT+Biochem)		30th Dec
31th - Dec - Break		
Anatomy (Dr. Shrinkant)	1st Jan - 5th Jan	6th Jan
Microbiology (Dr. Priyanka Sachdev)	7th Jan - 10th Jan	11th Jan
BTR E&D (Anatomy + Microbiology)		12th Jan
13th - Jan - Break		
Psychiatry (Dr. Praveen Tripathi)	14th Jan - 15th Jan	16th Jan
Ophthalmology (Dr. Gaurav Nagpal)	17th-20th Jan	
ENT (Dr. Praneeth)	21th-24th Jan	
Combined E&D (Ophtha + ENT)		25th Jan
BTR E&D (Psy/Oph/ENT) (Dr. Zainab Vora)		26th Jan
Radiology (Dr. Zainab Vora)	27th Jan - 28th Jan	

SWIPE LEFT

Topic	Date	E&D
Orthopedics (Dr. Apurv Mehra)	29th Jan - 30th Jan	
Combined E&D (Radiology + Orthopedics)		31st Jan
Surgery (Dr. Amrit Nasta)	1st Feb - 4th Feb	
5th - Feb - Break		
Surgery-2 (Dr. Amrit Nasta)	6th Feb - 8th Feb	9th Feb
BTR E&D (Surgery/Ortho/Radio) (Dr. Zainab Vora)		10th Feb
PSM-1 (Dr. Vivek Jain)	11th-13th Feb	
14th - Feb - Break		
PSM (Dr. Vivek Jain)	15th-17th Feb	18th Feb
Anesthesia (Dr. Jhanvi Bajaj)	19th-20th Feb	
Dermatology (Dr. M.Srinivas)	21st-22nd Feb	
Combined E&D (Anesthesia + Dermatology)		23th Feb

SWIPE LEFT

Cerebellum

Topic	Date	E&D
BTR E&D (PSM/Anes/Derma) (Dr. Zainab Vora)		24th Feb
Pediatrics (Dr. Anand Bhatia)	25th Feb - 27th Feb	28th Feb
OBG-1 (Dr. Raina Chawla)	1st Mar - 4th Mar	
5th - Mar - Break		
OBG-2 (Dr. Raina Chawla)	6th-7th Mar	8th Mar
BTR E&D (Pediatrics/OBG) (Dr. Zainab Vora)		9th Mar

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2nd - Mar - Break

SWIPE LEFT

Cerebellum

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