NEPHROLOGY

Dr. Rahul Rajeev

URINE ANALYSIS

physical → chemical → Microscopy

Prefered sample – Morning Midstream sample
To be tested within 2-4 hours
Refrigeneration at 4-8°C

Polyuria – Urine output >3L/day , >40ml/kg . >50ml/kg
→ With Urine Osmolality <250 mosml/kg → Diabetes insipidus
→ with Urine Osmolality > 300 mosml/kg - Primary polydipsia (Psychogenic polydipsia)
(solute) solute diuresis - Glucose, mannitol,
also loss (Diabetes Melitus) Radiocontrast.
Resolving phase of acute tubular necrosis (ATN)

Urine osmolality - mosm/kg
osmalarity - mosm/l

50-1200

Oligoria - U/o <400ml/day
Anuria - urine output <100ml/day

Specific gravity : 1.003 - 1.03
Isosthenuria - fixed specific gravity
CKD

pH - 4.5 - 8
Protein, ketone, glucose, bilirubin - Negative

Microscopic analysis → centrifuged sample (cells, cast, crystals)
cells : RBC nil → 1-2/hpf ≥3 RBC/hpf Hematuria.
WBC ≤4/hpf ≥5/hpf pyuria - UTI

sterile pyuria → Pyuria + negative bacterial culture.
TB, Atypical organism, SLE, fungal infections, Renal calculi, Acute interstitial Nephritis (AIN)

Eosinophils - nil → Eosinophiluria
AIN, Atheroembolic renal disease.
manifestn with cholestrol embolism in the kidney.
leads to AKI

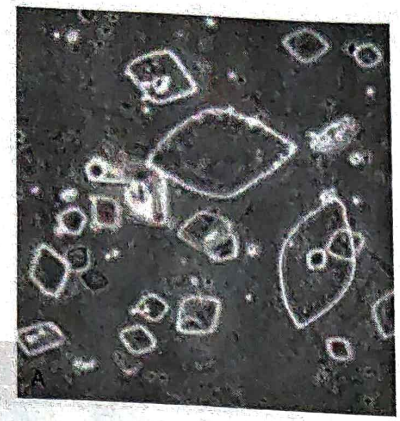
Fat bodies - Nephrotic Syndrome
"Maltese cross" appearance - (Babesha)
(Hollenhorst plaque - eg:)
↳ cholesterol material blocks retinal artery

Cast	Clinical association
Hyaline	Normal individual, Renal disease
Granular	Renal disease
Muddy brown granular	Acute Tubular Necrosis
Waxy	Renal disease
Broad waxy	Chronic Kidney Disease
Fatty	Nephrotic syndrome
RBC	Acute Glomerulonephritis Acute Interstitial nephritis
WBC	Acute Pyelonephritis Acute Interstitial nephritis
Epithelial	Acute Glomerulonephritis Acute Pyelonephritis Acute Interstitial nephritis
Myoglobin	Rhabdomyolysis

Crystals

Calcium Oxalate

dihydrate



Rhomboid shape.
– Uric acid

monohydrate



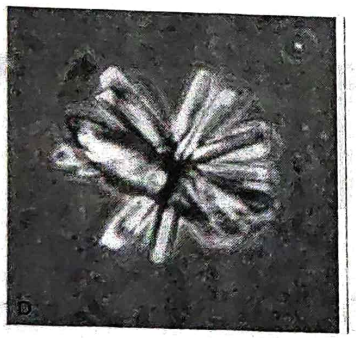
Envelope shape



Dumbell shape.

– calcium phosphate

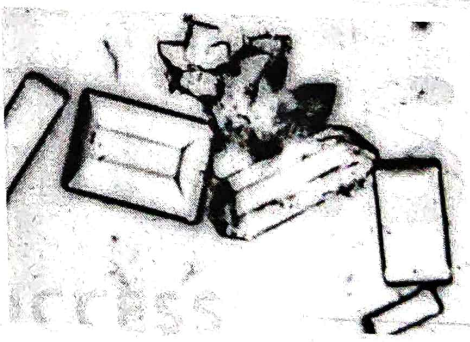
star

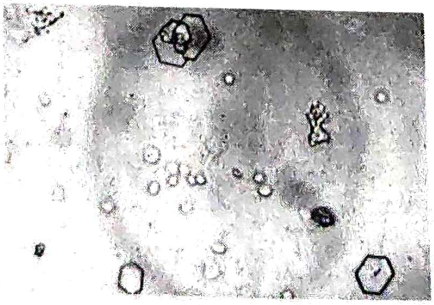


magnesium ammonium phosphate

Triple phosphate / struvite

Coffinlid shape





Hexagonal – cystine

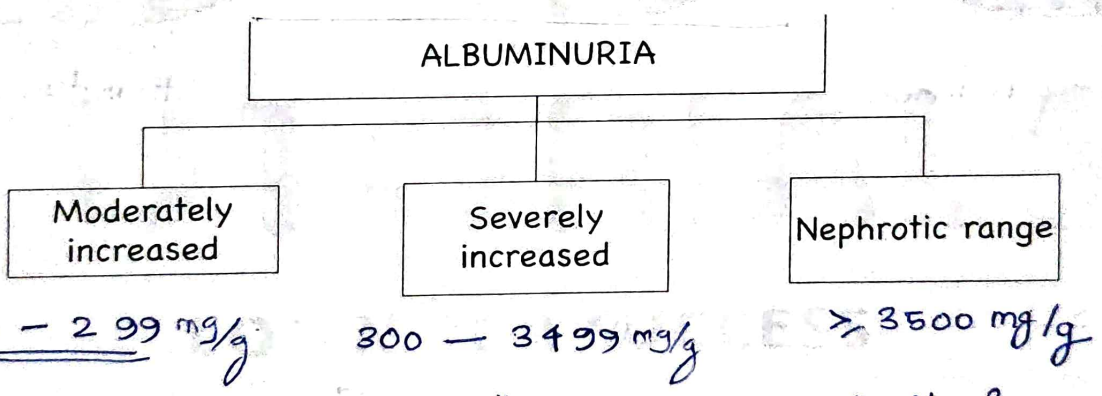
APPROACH TO PROTEINURIA

Normal: <30mg/24h.

- Urinary protein in a normal healthy individual <150mg/24hour
- Urinary proteins THP (Gamm horsefall protein), Albumin, Urokinase, secretory IgA, β-2micro globulin
- Dipstick method – only measures albumin – Nil
  - sulfosalicylic acid test – Total protein
- Quantitative assessment
  - ✓ 24 hour Urinary protein (albumin) assessment – AER – Albumin excretion rate. mg/24hr
  - ✓ spot urinary protein creatinine ratio – PCR.
    albumin ... ACR. mg/g

ACR
T 30mg/g

AER
≥30mg/day



Microalbuminuria
- early diabetes
- Essential hypertension
- Early stages of glomerulo nephritis

Macroalbuminuria.
same
+
myeloma kidney

Nephrotic Syndrome
- 1°: MCD, FSGS, membranous nephropathy
- 2°: Diabetes, Amyloidosis

APPROACH TO HEMATURIA

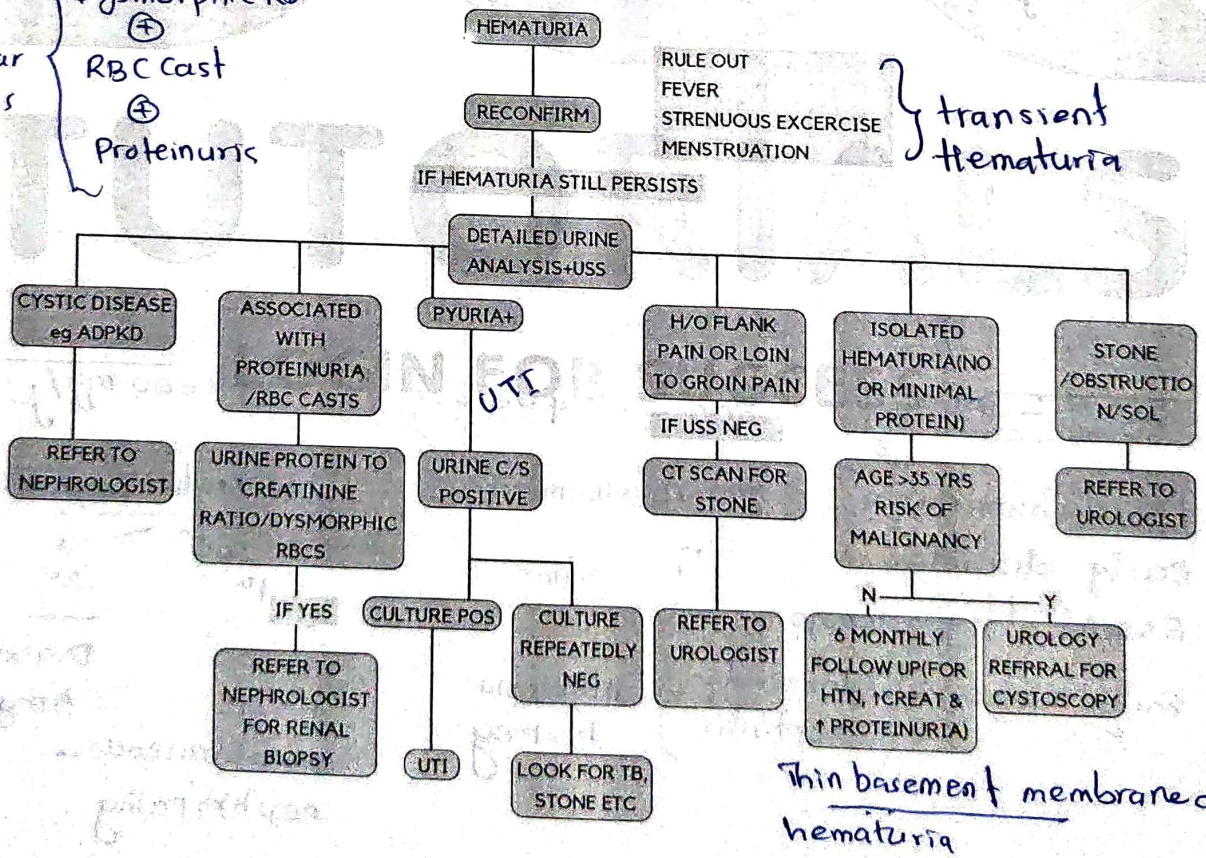
- Normal urine 0-2/0-3
- Significant hematuria ≥3 RBC's/hpf on 3 urine sample.
  ≥ 100 RBC's/hpf on 1 urine sample.
  Gross hematuria.

CAUSES OF HEMATURIA

Lower Urinary Tract
- Cystitis
- Ca Bladder
- Renal calculi

Upper Urinary Tract
- Glomerulonephritis
- Renal cell carcinoma
- Renal calculi
- Pyelonephritis

Glomerular Nephritis:
- Dysmorphic RBC
- ⊕ RBC Cast
- ⊕ Proteinuria



Thin basement membrane disease
hematuria

ACUTE KIDNEY INJURY

- Absolute increase in serum creatinine by ≥ 0.3 mg/dL over 48 hours,

  OR

  Relative increase ~~of~~ to ≥ 1.5 times within 7 days

Urea - 20-40mg/dl
creatinine - 0.7-1.4mg/dl

Staging of AKI is based on serum creatinine and urine output

Stage	Serum creatinine	Urine output
Stage 1	1.5 -1.9 times	less than 0.5ml/kg/hr for 6-12hours
Stage 2	2 - 2.9 times	less than 0.5ml/kg/hr for >12hours
Stage 3	≥ 3 times	less than 0.3ml/kg/hr for >24hours

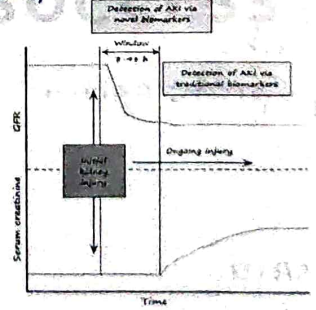
or anuria >12hour
Dialysis requirment.

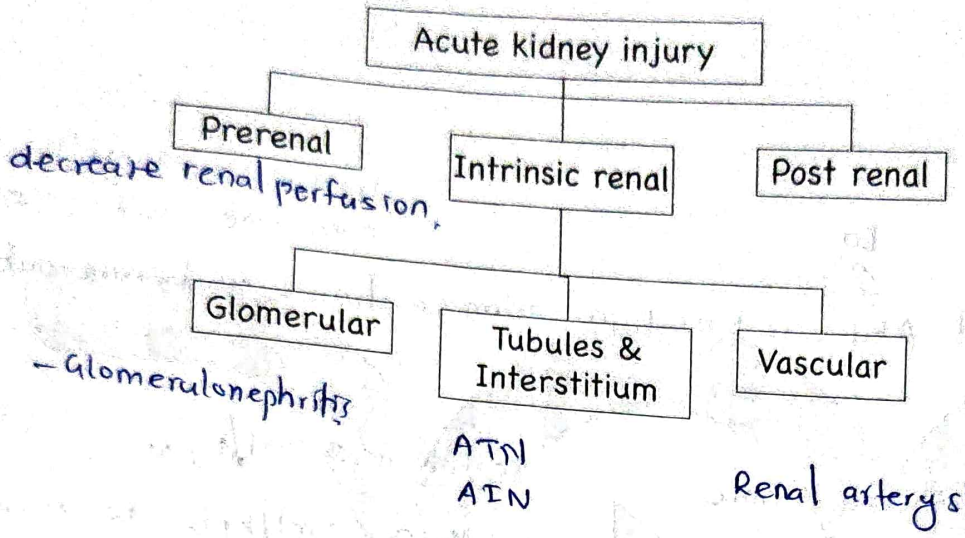
Novel Biomarkers for AKI

→ used to detect AKI in window period.

- NGAL (Neutrophil gelatinase arrosiated (lipocalcin)
- KIM-1 kidney injury molecule -1
- IL-18
- Osteopontin
- Cystatin C
- Liver type ~~FBAP~~ FABP

Fatty acid Binding protein





decreate renal perfusion

- Glomerulonephritis

ATN
AIN

Renal artery stenosis

m/c CAUSES OF PRE-RENAL AKI

- Volume depletion - G.I fluid loss, Blood loss
  Excess diuretic use

- Volume overload with reduced renal perfusion
  CCF, liver cirrhosis
  severe hypoproteinemia

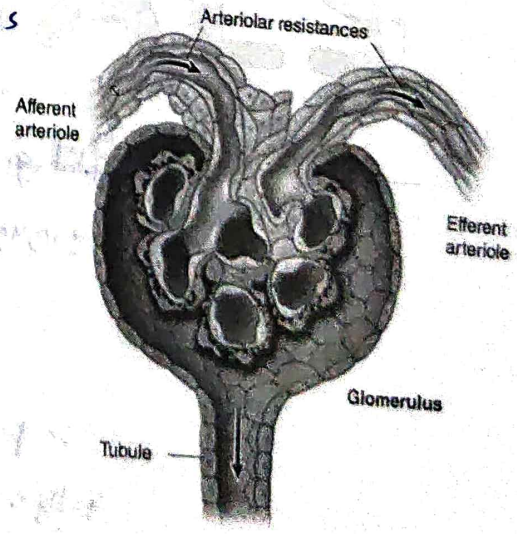
CCF
↓
volume forward failure
↓
kidney perfusion ↓
↓
RAAS
↓
volume overload

- Renovascular disease

Drugs - NSAID ⊖ → Prostaglandin - V.D

ACE I / ARB → CA ad ↓ → V.D

cyclosporine



Dr. Rahul Rajput
TUTORIALS

Acute Tubular Necrosis

- Infection/Sepsis
- Nephrotoxins
  - Exogenous
    - Iodinated contrast.
    - Drugs: Aminoglycosides, cisplatin, proton pump inhibitor, Amphotericin B, NSAID
    - Ethylene glycol
    - Snake bite.
  - Endogenous
    - Myoglobin – Rhabdomyolysis
    - Hemoglobin – Hemolysis
    - (multiple Myeloma) light chains.
    - Uric acid – Tumor lysis Syndrome
      - TLS Rx → Rasburicase.
      - ALL, Burkitt's lymphoma – High grade turnover.
      - chemotherapy → rapid cell death
      - ↑↑ Purine release → Uric acid
      - ↓ Uric acid/ Urate nephropa
- Ischemia

↳ non oliguric AKI

- Contrast induced nephropathy

Elderly, dehydration, anemia, CKD → risk of contrast induced nephropathy

!! ✓ Ionic high osmolar contrast
non ionic low osmolar contrast

→ 24–48 hour → creatinine begin to raise
3–4 days → creatinine peaks
One week → return back to normal.

- Drug induced ATN

ATN
- Initiation phase
- Maintenance phase
- Recovery (all new age cells)
  → Polyuria, solute diuresis
  → Recovery phase of ATN →

Prevention
- Hydration
- oral NAC (N-acetylcysteine)
- sodium bicarbonate
- non-ionic low osmolar contrast

ACUTE INTERSTITIAL NEPHRITIS

(Allergic interstitial)

- Drugs — Antibiotics — Blactam antibiotics, sulfonamides, quinolones, vancomycin.
  NSAIDs
  Diuretics
  Anticonvulsants
  PPI
- Infections → Streptococcal, EBV, Leptospirosis, mycoplasma
- Classic triad — Fever + rash + arthralgia — eosinophilia +/- eosinophiluria

CLINICAL FEATURES

- Asymptomatic → Deranged RFT — Azotemia → uremia
- Decreased urine output — nonoliguria → oliguria → Anuric
  polyuria - recovery phase of ATN
- Uremia — uremic toxins
  Nausea, vomiting, hiccoughs, itching
  uremic pericarditis, uremic encephalopathy, bleeding tendancy
- Symptoms & signs of underlying disorder
  Fever, rash, arthalgia - AIN
  Dehydration; Prerenal AKI
- Hypertension — activation of RAAS
- Impaired fluid homeostasis
  periorbital edema, puffiness of face, pedal edema, anasarca

INVESTIGATIONS

- RFT → ↑ in urea / creatinine
- Urinalysis Glomerulonephritis — Dymorphic RBC, RBC cast, Proteinuria.
  AIN - Eosinophils, WBC cast.
- Electrolytes – ↓ Na^+, ↓ Ca^{2+}, ↑ PO_4^{3-}, ↑ K^+
- ABG – metabolic acidosis
- ECG – electrolyte Abnormality.
- USG, CT Abdomen – post renal AKI

Uric acid – Hyperuricemia.

BUN - ½ Blood urea.

$$FeNa = \frac{UNa^+}{Plasma\ Na^+} \times \frac{P\ creatinine}{Urine\ creatinine}$$

PRE-RENAL AKI VERSUS ATN

Parameter	Pre-renal AKI	Acute Tubular Necrosis
BUN/Plasma creatinine	> 20 : 1	10-15 : 1
Urine osmolality (mosm/l)	> 500	< 350
Urine sodium (meq/l)	< 20	> 40
FeNa (%)	< 1	> 2
Cast	None or Hyaline	Muddy brown granular

TREATMENT OF AKI

- Fluid balance — Dehydration – I.V fluids → Fluid restriction
  Fluid overload – diuretics — I = O + 500ml (input = output + insensible loss)

- Correction of electrolyte imbalances

  Hyponatremia – Fluid restriction, Avoid hypotonic fluids

  Hyperkalemia – calcium gluconate (membrane stabilization), insulin + dextrose, salbutamol, Potassium binding resins (Patiromer)

  Hyperphosphatemia – Dietary phosphate restrictions
  ↳ Phosphate binder.
  – calcium acetate
  ca carbonate
  Sevelamer
  Lanthanum.

  Hyperuricemia – Febuxostat

  Metabolic acidosis – sodium bicarbonate

- Treat underlying cause

  AIN – Stop offending drug → improvement
  ↳ steroid

  TLS – Rasburricase

  Treat associated condition like hypertension.

- Indications for dialysis

  (A)cid- base or (E)lectrolyte disturbances refractory to medical management

  (I)ntoxications from certain drugs – Ethylene glycol, Lithium,

  volume (O)verload unresponsive to diuretics

  (U)remic complications

  ↳ encephalopathy.
  → pericarditis

CHRONIC KIDNEY DISEASE

- Progressive affection of kidney structure or function (> 3 months)

Primary glomerular diseases	Secondary glomerular diseases	Tubulointerstitial nephritis
IgA Nephropathy	Diabetes, SLE	NSAID (Analgesic Nephropathy) → Phenacitin (contain preparation), sickle cell disease

Cystic diseases	Obstructive nephropathies	Vascular diseases
ADPKD, ARPKD	Bladder outlet (BOO) obstruction, Nephrolithiasis	Hypertension, Renal artery stenosis

Criteria for CKD (either of the following present for > 3 months)	
Markers of kidney damage (one or more)	- Albuminuria (AER ≥ 30 mg/24 hours; ACR ≥ 30 mg/g)
	- Urine sediment abnormalities — RBC cast, Dysmorphic RBC
	- Electrolyte and other abnormalities due to tubular disorders — RTA (Renal tubular acidosis), Bartter's Syndrome
	- Abnormalities detected by histology "wire loop lesion"
	- Structural abnormalities detected by imaging — ADPKD
	- History of kidney transplantation
Decreased GFR	- GFR < 60 ml/min/1.73 m^2 (GFR categories G3a-G5)

GFR

- Amount of plasma ultrafiltered across filtration barrier per unit time
- Normal GFR – 125 ml/min /1.73 m^2

- GFR measurement

✓ Inulin clearance – Gold standard

✓ Creatinine clearance – Clearance of endogenous creatinine

↳ Cockcroft : Gault Formula

eGFR → CKD-EPI equation ✓✓

MDRD Formula

⊙eGFR – Age, Sex, Weight, Creatinine

- Cystatin C – independent of muscle mass

STAGING OF CKD

- Based on GFR

Early stage of diabetic Nephropathy
Glomerular hyperfiltration

Stage	Description	GFR
G1	Normal or ↑GFR	≥ 90
G2	Mildly reduced GFR.	60-89
G3a	Mild - moderately reduced GFR	45-59.
G3b	Moderate - severly reduced GFR.	30-44
G4	Severly reduced GFR	15 - 29.
G5	ESRD	<15

- Based on albumin excretion

A1 < 30mg/g

A2 30 - 299 - micro albuminuria

A3 ≥ 300. - macro albuminuria.

CLINICAL FEATURES

- Asymptomatic
- Decreased urine output - oliguria → Anuria
- Uremia - Nausea, vomiting, Itching
  encephalopathy, Pericarditis, bleeding tendernessn cle
- Symptoms & signs of underlying disorder DM- retinopathy, cataract.
  SLE-malar rash.
- Hypertension
- Impaired fluid homeostasis, electrolyte imbalances, acid base disorder

periorbital puffiness
pedal edema.
Ascites
Anacarca.
Pulmonary edema.

Metabolic acidosis
CHAGMAD

Renal osteodystrophy, Mineral Bone disease.

Bone Manifestations

High bone turnover

- GFR ↓ also Osteitis fibrosa cystica
- Phosphate (PO_4^{3-}) ↑
- Osteocyte → FGF-23 (Fibroblast growth factor) → phosphaturic
- inhibit → 1-α hydroxylase
- Decrease in activated vitamin D
- ↓ serum calcium
- ↑ PTH → 2° Hyperparathyroidism
- ↑ PTH
- ↓ Ca^{2+}
- ↑ FGF-23
- ↓ $1,25(OH)_2D_3$ ← ↑ P
- Chronic Kidney Disease

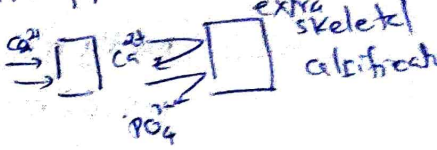
Osteomalacia

- → vitamin D deficiency
- ↓
- defective mineralisation of bone matrix

Low bone turnover

a.k.a adynamic bone dz.

- → Iatrogenic
- Vitamin D supplements, Ca^{2+} containing phosphate binders.
- → PTH suppression



Both FGF-23 & PTH are phosphaturic

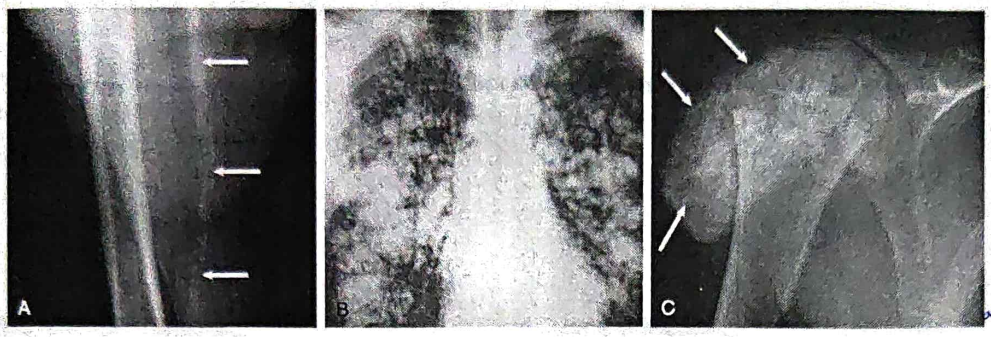
- ↓ Subperiosteal resorption of n. radial aspect of phalanga.
- → Salt and Pepper skull
- Rugger jersy spine.
- ↘ osteoclastic activation
- ↓
- Lytic lesion in bone
- expansile lytic lesion
- central area → Area of hemorrhage & Necrosis → Brown colour "Brown tumor"

Von Recklinghausen disease of bone.

→ Unlike High bone turnover disease Osteomalacia this Iatrogenic due to excessive use of vitamin D supplements and Ca^{2+} in a patient with chronic kidney disease.

Extra skeletal calcification.

Blood vessel Lungs Peri-articular soft tissue



CKD pt taking warfarin, expose to ↓ calcium

Calciphylaxis / Calcific uremic arteriolopathy



CKD → 2° hyperparathyroidism → Excess intake of Ca^{2+}/vitamin D supplement

Tumoral calcinosis

PTH suppression → vascular lumen narrowing → Erythema, Gangrene.

CARDIOVASCULAR MANIFESTATIONS

- Hypertension → RAAS
- CAD
- Heart failure
- Arrhythmias
- Pericarditis

NEUROLOGICAL MANIFESTATIONS

- CNS, PNS, ANS → Autonomic dysfunction (→ peripheral neuropathy)
  - ↓
  - Uremic encephalopathy
  - Restless leg syndrome

HEMATOLOGICAL MANIFESTATIONS

- Anemia → Peritubular capillaries Normocytic Normochromic anemic
  - Erythropoietin deficiency
  - Diminished RBC survival
  - Bleeding diathesis
  - Iron deficiency
  - Hyperparathyroidism → Bone marrow fibrosis
  - Chronic inflammation
  - Folate/Vitamin B12 deficiency
  - Hemoglobinopathy
    CKD dlt → sickle cell anemia

Uremia → Platelet dysfunction
↓
inhibit clotting factor

- Coagulopathy ↓ level of clotting factors
  lead to bleeding tendencies

DERMATOLOGICAL MANIFESTATIONS

Pruritis
Pigmentation – urochrome

- Nephrogenic systemic fibrosis
  in MRI use gadolinium lead to skin thickening

Patients with CKD stage 3 should minimize exposure to gadolinium and those with CKD stages 4–5 should avoid the use of gadolinium agents

("Albumin is tubulotoxic")

Peau d orange appearance.





dk melanin deposition

OTHER MANIFESTATIONS

Nail — Lindsay nail
or Half - Half nail.

Investigation : Same as AKI, Serum Ca^{2+}, vitamin D, PTH.
USG — Loss of CMD. (Corticomedullary differentiation)

TREATMENT OF CKD

- Slowing progression — Treat underlying cause (SLE, DM, HTN)
  anti proteinuric agents (ACE I, ARB, SGLT2 inhibitors)
  avoid nephrotoxic drugs
  Management of cv risk factors

- Dietary management

Protein restriction 0.6-0.8 g/kg/day.

Salt & water restriction → 2-3g/day
To avoid fluid overload

Potassium restriction

Phosphorus restriction → MBD.

↓ intake of phosphorus containing foods
canned foods

Phosphate binders

Ca^{2+} containing
Calcium acetate
calcium phosphate

without calcium → sevelamer
Lanthanum

Other

- Management of clinical manifestations

Anemia – Recombinant human erythropoietin

Darbepoietin alfa
Epoietin alfa
} ESA (erythropoeitn stimulation Agents)

Iron supplementation.

Hb target : 10-11.5 g/dl.

Hyperkalemia

Metabolic acidosis – sodium bicarbonate oral or iv.

Hyper uricemia – Febuxostat.

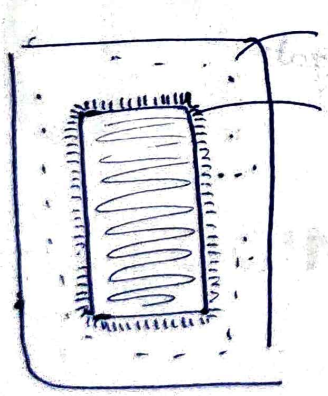
• Treatment of ESRD → Renal replacement therapy → ESRD / severe AKI

Types of ~~AKI~~ RRT — Hemodialysis (dialysis), Peritoneal dialysis, Renal transplantation

Indications of dialysis

1. Refractory Fluid overload
2. Oliguria / Anuria not responding to medical management
3. Refractory hyperkalemia
4. ~~Sodium~~ Refractory metabolic acidosis
5. Refractory hypertension.
6. Uremic complications - encephalopathy, pericarditis

Hemodialysis



3-5 hours:

HEMODIALYSIS

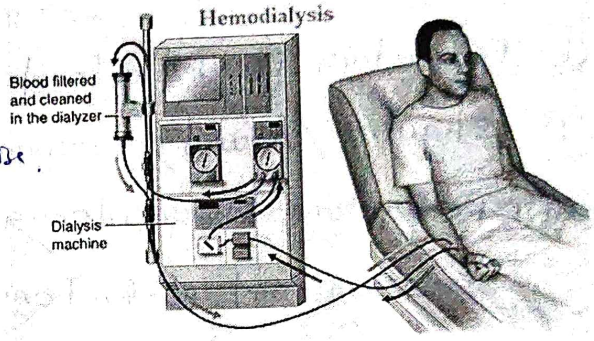
- Temporary dialysis - IJV - tunneled catheter (6-8 weeks)
- Permanent ~~hemo~~ - AV Fistula / prosthetic graft → (2 weeks)

- 3 essential components : Dialyzer, Dialysate, Blood delivery system

Intermittent hemodialysis - 3 days per week.

SLED - Sustained low efficiency dialysis 6-12 hours
- chronic kidneys patient with high probability of hemodynamic compromise.

CRRT - continuous renal replacement therapy.
AKI with hypotension require dialysis.



complication: hypotension, muscle cramps, Bacteremia → sepsis, DDS - dialysis disequilibrium syndrome
- first time initiation
- after skipping dialysis session

→ cerebral edema

& mannitol

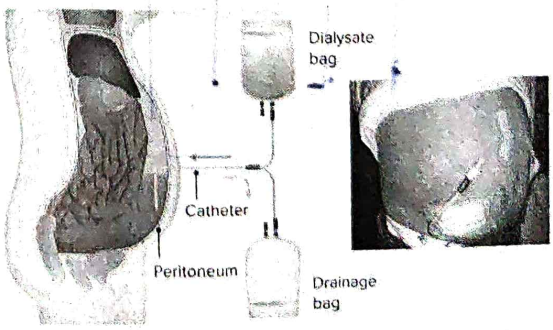
Dialysis done ~~daily~~ daily

PERITONEAL DIALYSIS

- Peritoneal membrane is the dialyzer → Dialyzate.
- 1.5-3 L of dextrose-containing solution is infused into the peritoneal cavity
- Allowed to dwell for a set period of time, usually 2-4 h

- CAPD continuous ambulatory peritoneal dialysis

- CCPD continuous cyclic peritoneal dialysis



Complication : Peritonitis
catheter site infection

RENAL TRANSPLANTATION

- Treatment of choice for ESRD

- Factors influencing graft survival
  - HLA mismatch
  - Very young or older donor age
  - African-American donor/recipient
  - Female donor sex
  - Older recipient age
  - Presensitization

CONTRAINDICATIONS

- Active glomerulonephritis
- Active infection
- Active malignancy
- Active hepatitis
- Overt AIDS

REJECTION

- Hyperacute - Immediate graft rejection due to presensitization
- Acute - Occurring within weeks to months
- Treatment - Pulse methylprednisolone

calcineurin inhibitors.

IMMUNOSUPPRESSION

Oral steroids
CNI - cyclosporine, Tacrolimus
MMF
Azathioprine

OPPURTUNISTIC INFECTIONS

- Peri-transplant [< 1month] - wound infection, herpes infection, oral candidiasis
- Early 1-6months - CMV, P. carini, Legionella, Hep B & C
- Late >6months - Aspergillus, Nocardia, polyomavirus [BK virus]

RENAL ARTERY STENOSIS

- Etiology: Atherosclerosis (m.c, elderly), Takayasu arteritis (indra, young patients), Fibromuscular dysplasia (worldwide)

RAAS activation → Refractory hypertension and its complication.

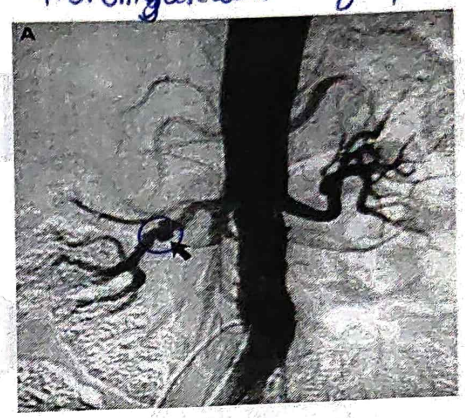
- Clinical features: AKI → CKD
  Renal bruit
- Investigations: Renal artery doppler, USG of kidney
  MRA / CTA / DSA.
- Treatment: Medical management, Angioplasty with stenting

U/L RAS → ACEI/ARB, D.O.C
BL ARB → ACEI/ARB is contraindicated.
CCB.

Atherosclerosis DSA

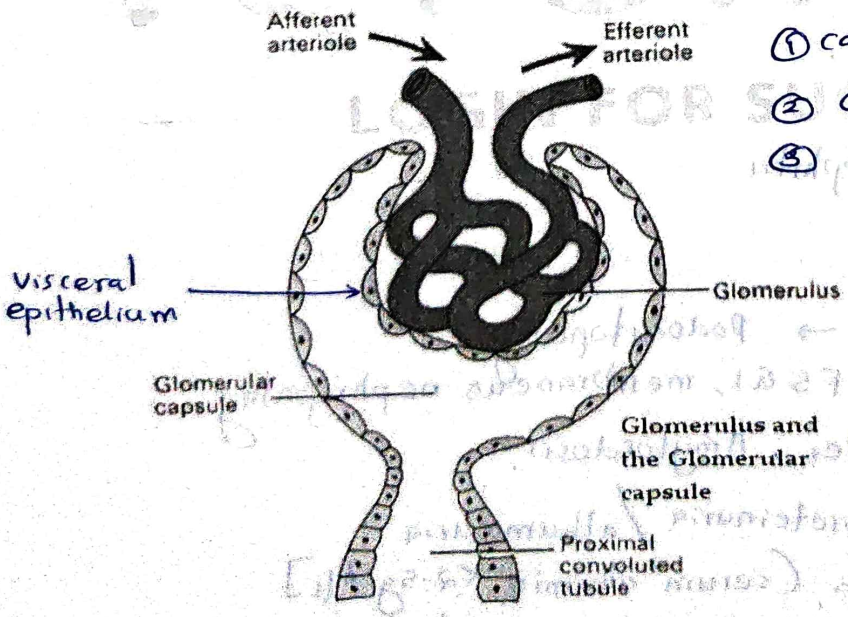


Fibromyuscular dysplasia.



Beaded string

GLOMERULAR DISORDERS

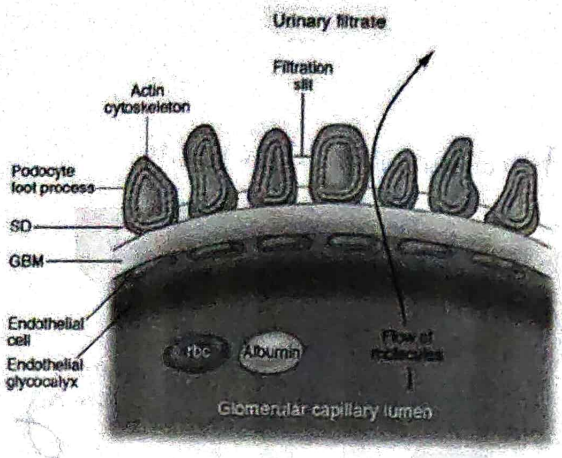


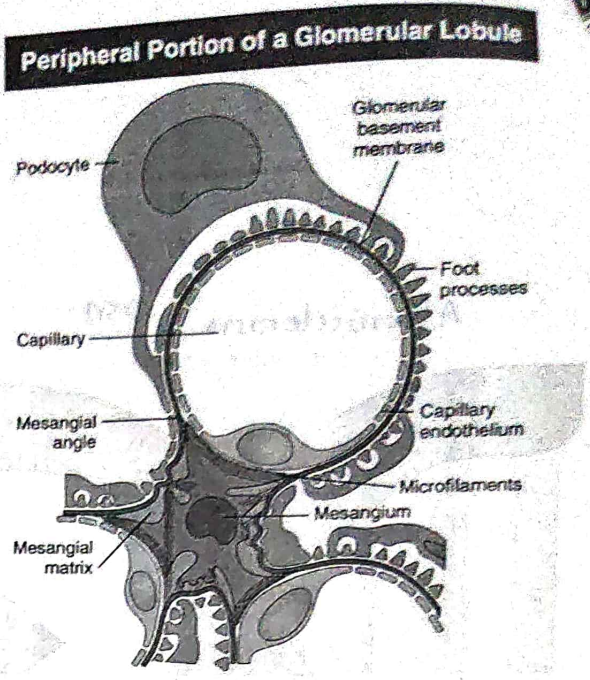
Glomerular Filtration Barrier

1. capillary endothelium } prevent hematuria,
2. GBM
3. visceral epithelium of B.M. ↳ prevent proteinuria

↓

Also called podocytes //





CLINICAL PRESENTATIONS

1. Asymptomatic (microscopic hematuria)
2. Macroscopic hematuria
3. Nephritic Syndrome.
4. Nephrotic Syndrome.
5. RPGN
6. chronic glomerulonephritis

NEPHROTIC SYNDROME

Damage to podocytes → Podocytopathy

LONS → MCD, FSGS, membranous nephropathy

2°NS → Diabetes, Amyloidosis.

1. Nephrotic range proteinuria / albuminuria
2. Hypoalbuminemia (serum albumin <2.5g/dl)
3. Edema +++ (Hypoalbuminemia → ↓oncotic pressure. sodium & water result ~~error~~ retension > Hypoalbuminemia)

periorbital puffiness → pedal edema → ascites, Anasarca.

④ Hyperlipidemia.
⑤ Lipiduria.

Increase risk of thrombotic events. (Urinary loss of antithrombin III)

NEPHRITIC SYNDROME

Damage to capillary endothelium & GBM.

① Hematuria
② Hypertension.
③ Oliguria
④ Proteinuria.
⑤ Edema. ④

RPGN

- Rapid decline in GFR
- Biopsy - Proliferative GN with crescents.

① Good pasture syndrome
② SLE - lupus nephritis
③ Wegner's granulomatosis. [GPA] granulomatosis with polyangiitis

FEATURES	NEPHROTIC	NEPHRITIC
Onset	Insidious	Abrupt
Edema	+++	+
Blood Pressure	Normal	BP raised
JVP	Normal / low	Raised.
Proteinuria	Nephrotic range.	Nephritic range.
Hematuria	Absent	Present
RBC casts	Absent	Present
Serum albumin	low	Normal / slightly reduced.

MINIMAL CHANGE DISEASE

- Most common cause of nephrotic syndrome in children
- Primary, Secondary → URTI, Hodgkin's ds, Drugs (Lithium, NSAIDs)

CLINICAL FEATURES

Nephrotic syndrome.

INVESTIGATIONS – Selective proteinuria (→ Albumin), Renal biopsy

LM, IM → Normal
EM → Effacement of foot process
(filtration slit become more permeable)

TREATMENT

Steroids
Frequent relapse / Steroid resistance → cyclophosphamide, CNI, Rituximab.
(calcineurin Inhibitor)

FOCAL SEGMENTAL GLOMERULOSCLEROSIS

- Most common cause of nephrotic syndrome in adults
- Primary, Secondary → VUR (vesicoureteric reflex), drugs, Bisphosphonates
  ↓
  APOL1 polymorphism,

CLINICAL FEATURES

Nephrotic Syndrome
Hypertension, Renal impairment, Hematuria

INVESTIGATIONS Renal Biopsy

LM – Sclerosis of some glomeruli
IM – IgM & C3 deposition in sclerotic area
EM → Foot process effacement

TREATMENT

→ Steroids
→ Cyclosporine
→ ACEI / ARB.

MEMBRANOUS NEPHROPATHY

- Most common cause of nephrotic syndrome in elderly
- Primary, Secondary → SLE, Infection like Hep B&C, Endocarditis, malignancies, Drugs (NSAID's, Penicillamine)
  - ↳ Anti PLA_2 Receptor. (Lung, Breast, colon)

CLINICAL FEATURES

Nephrotic Syndrome
Highest risk of thrombosis.

INVESTIGATIONS Renal Biopsy

LM → uniform thickening of GBM.
Silver methinamine stain
↓
Spike and dome pattern.
IM → Diffuse granular deposit of Ig G and C_3.
EM → Electron dense subepithelial deposits.

TREATMENT

Steroid, Cyclophosphamide, Cyclosporine, Rituximab
⊕ ACEI/ARB.

MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS

a.k.a. • Mesangiocapillary glomerulonephritis MPGN

- Secondary → Hep B/C, Guaiatan malaria, SLE
  Cryoglobinemia, monoclonal gammapathies.

CLINICAL FEATURES

MPGN

Type I
Immune complex mediated

Type II
Complement Mediated
C_3 glomerulopathy

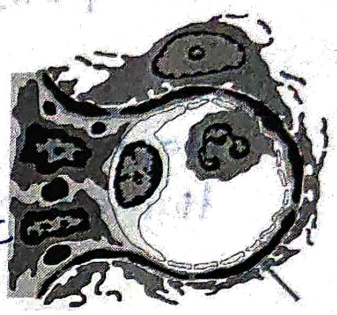
Dense deposit disease.
Intramembraneous deposits ⊕
Intramembraneous deposits ⊖

- Nephrotic syndrome
- Nephrotic + Nephritic
- Nephritic
- R PGN
- CGN (chronic glomerulonephritis)

INVESTIGATIONS

Renal biopsy

LM - mesangial proliferation, lobulation of glomerular tuft



Immunofluorescent microscopy - IgG & IgM deposits

EM - GBM spliting (Tram track appearances) split of glomerular basement membrane by immune complex deposit.

C3 deposit

TREATMENT

Steroids

Treat underlying cause.

ACEI / ARB.

PSGN POSTINFECTIOUS GLOMERULONEPHRITIS (streptococcal)

- Most common cause of nephritic syndrome in childhood
- 1-3 weeks after pharyngeal (sore throat) or cutaneous (impetigo) infection
  - 2 - 6 weeks
- Nephritogenic strain of streptococci

CLINICAL FEATURES

Nephritic syndrome, cola coloured urine

RPGN - some care. (rare)

Serum C_3 ↓, Serum C_4 (N) → PSGN
Serum C_3 ↓↓ Serum C_4 ↓ ■ → SLE
Lupus nephritis

INVESTIGATIONS

- Serum C3, anti DNAse B, ASO titer
  ↳Reduced. elevated elevated.
- Renal biopsy LM – Enlarged glomeruli with proliferative pattern.
  IM – Granular deposition of IgG & C_3 in mesangium.
  EM – subepithelral humps.

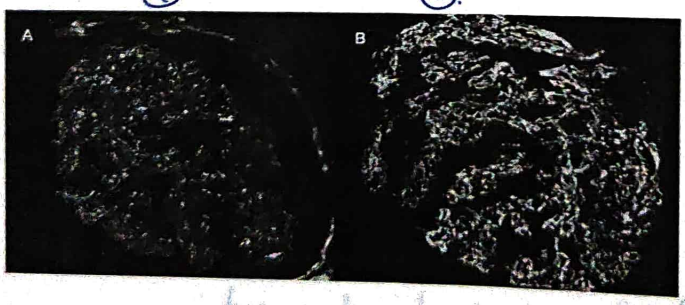
TREATMENT

Similar to AKI – supportive.
No role of steroids
Antibiotics ↓Active infection.

① (N)



②



① Starry sky appearance children.

② Garland pattern – adults

→ Berger's disease.

IgA NEPHROPATHY

- Most common primary glomerular disorder worldwide
- Secondary – liver cirrhosis, Hiv, CMV
- Mesangial deposition of immune complexes — Aberrantly glycosdated IgA

CLINICAL FEATURES

- Age group 2nd to 3rd decade, M>F. Trigger – URTI
  - ↓ 1- 3 days
  - Asymptomatic
  - Macroscopic hematuria. — Synpharyngitic hematuria.
  - Nephrotic Syndrome
  - Nephritic Syndrome
  - RPGN
  - CGN

1/3rd → Nephrotic (Leptodic hematuria)
1/3rd → CGN
1/3rd → spontaneous resolution.

INVESTIGATIONS

Renal biopsy. – IM.: diffuse mesangial IgA & C3 deposits

TREATMENT

ACEI/ARB, SGLT2 inhibitor, Sparsentan, Steroids

- ↓ Dapagliflosin.
- ↓ dual antagonist
  - Endothelin
  - Angiotensin II receptor.

α_3 NCD

GOODPASTURE SYNDROME - GPS.

Non collagenous domain.

- Antibodies against NCD of type IV collagen

- Trigger — infection, Tobacco use.

Pulmonary Renal
C-ANCA +ve: WG
P-ANCA +ve: Microscopic Polyangiitis
ANCA -ve: GPS

CLINICAL FEATURES

- Age group : Bimodal age group
  3rd decade, 6th–7th decade

- Pulmonary – Renal syndrome
  - Glomerulonephritis. → RPGN
  - Pulmonary capillaritis. — cough, dyspnea, hemoptysis.

INVESTIGATIONS

chest X-ray, CT thorax, PFT. → DLCO ↑
↓ infiltrates. ↓ infiltrates.

Renal Biopsy → LM → diffuse Alveolar Hemorrhage
Crescents
IM → Linear IgG staining along GBM.

TREATMENT

Steroids + plasma exchange (plasmapheresis)
cyclophosphamide

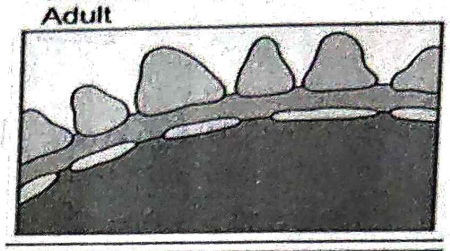
ALPORT SYNDROME

- Hereditary nephritis → Alport syndrome
  ↳ Thin BM ds.
- Genetics

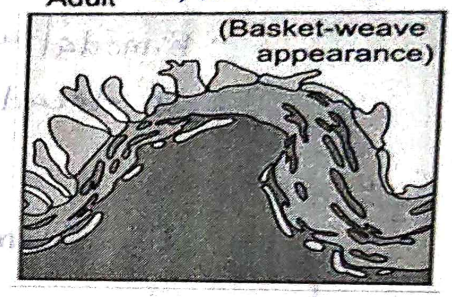
Gene mutation encoding Type IV collagen.

X-lined, AR, AD

α3α4α5 Heterotrimer.
Adult



α1α1α2
Adult → weak collagen → susceptibility to damage



CLINICAL FEATURES

- 1st decade — Microscopic hematuria
- 2nd decade — Nephritic
- 3rd decade — CKD.

- Alport versus Thin Basement Membrane disease
  ↓ Isolated hematuria

Extra-renal manifestations
SNHL, anterior lenticonus, Dot & fleck retinopathy → Anterior lenticonus

INVESTIGATIONS

Genetic analysis, Renal biopsy EM → diagnostic
- Non uniform thickness (area of thinning & thickening)
- Basket weave appearance

TREATMENT

ACE I / ARB
Renal transplantation.
↳ Does not recur after transplant.

DIABETIC NEPHROPATHY

- Common cause of secondary nephrotic syndrome

  Most Common Cause of CKD.

- Pathologic changes : Glomerular changes

  Capillary Basement membrane thickening, Diffuse mesangial sclerosis, Nodular glomerulosclerosis

  Most common renal lesion → Diffuse mesangial sclerosis

  Pathognomonic renal lesion — Nodular glomerular sclerosis [Kimmelstiel wilson lesion]

CLINICAL FEATURES

Glomerular : Microalbuminuria → CKD

Renal artery : Atherosclerosis → Renal artery stenosis

Pyelonephritis → Renal papillary Necrosis

Type IV RTA.

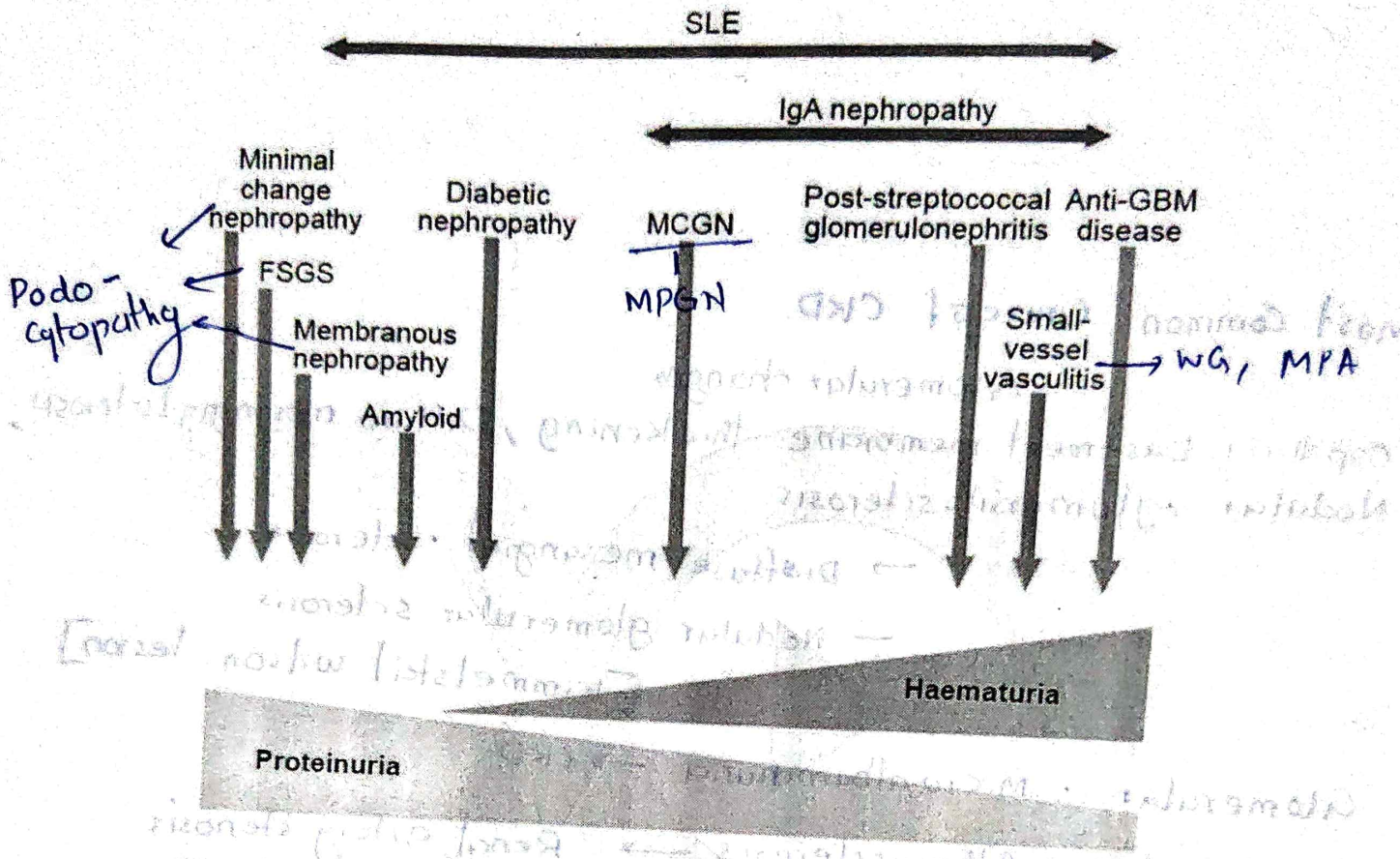
INVESTIGATIONS

Same as CKD.

TREATMENT

Glycemic control, BP control, ACEI/ARB, SGLT2I, MRA

↳ spironolactone



NEPHROLITHIASIS → Renal calculi

- Due to supersaturation of urine with insoluble components
- Stone composition → Relatively pH independent

✓ Calcium oxalate - Hypercalciuria and/or Hyperoxaluria

Calcium phosphate - In the setting of abnormally high urine pH

Struvite - Infection with urea splitting organisms. Stag horn calculi

Proteus, Klebsella

Uric acid - Uric acid in presence of acid urine pH

Cystine - Likely to form in acidic urine pH

CLINICAL FEATURES

Nausea, Vomiting

- Asymptomatic, Hematuria, Pain, Visceral symptoms, Pyuria, UTI

loin to Groin pain

INVESTIGATIONS

Urine analysis, Ultra Sound, NC CT-Abdomen (I.O.C)

TREATMENT

- Increase fluid intake. Low salt, Low fat, Moderate protein diet

Citrate supplementation

calcium >1200mg/day.

URINARY TRACT INFECTION – UTI

- UTI – Cystitis (Bladder), Pyelonephritis (Kidney), Prostatitis (Prostate), Asymptomatic bacteriuria

- Uncomplicated UTI versus Complicated UTI

Uncomplicated UTI – Acute disease in non pregnant outpatient women

(Complicated UTI – male, pregnant women).

- Microbiology

E.coli, Staph, Klebsiella, Proteus, Enterococcus, Gram positive bacteria

m.c.

CLINICAL FEATURES

- Asymptomatic bacteriuria - Incidentally detected
- Cystitis - Dysuria, Urinary frequency, Urgency, supra pubic discomfort, fever.
- Pyelonephritis - Fever, low back pain, nausea, vomiting

Papillary necrosis - Diabetes, Sickle cell disease, Analgesic nephropathy

Emphysematous pyelonephritis - Diabetes — peri-nephric area - gas formation.

Xanthogranulomatous pyelonephritis - Chronic obstruction + Infection

stag horn calculi

- Prostatitis - Fever, chills, dysuria, urinary frequency, BOO

INVESTIGATIONS

- Urinalysis
- Urine culture - Diagnostic gold standard
- Blood culture

Asymptomatic bacteriuria $>10^5$ bacteria/ml

cystitis $>10^3$ bacteria/ml.

CBC.

ESR ↑, CRP ↑.

Suspected Renal calculi
Suspected pyelonephritis
Recurrent UTI
} USG.

TREATMENT

- Uncomplicated cystitis in women - TMP-SMX, Nitrofurantoin 1-2 weeks
- Pyelonephritis - Fluoroquinolones
- UTI in pregnant women - Nitrofurantoin, Ampicillin, Cephalosporins
- UTI in men - Fluoroquinolones, TMP-SMX
- Asymptomatic bacteriuria - treatment only in special scenarios
  pregnancy
- Catheter Associated Urinary Tract Infection
  CAUTI - Remove catheter.

CYSTIC DISEASES OF KIDNEY

- Autosomal Dominant Polycystic Kidney Disease - ADPKD
- Autosomal Recessive Polycystic Kidney Disease - ARPKD
- Medullary Sponge Kidney - MSK
- Autosomal Dominant Tubulointerstitial Kidney Disease - ADTKD
- Nephronophthisis
- Tuberous Sclerosis
- Von Hippel Lindau syndrome

ADPKD

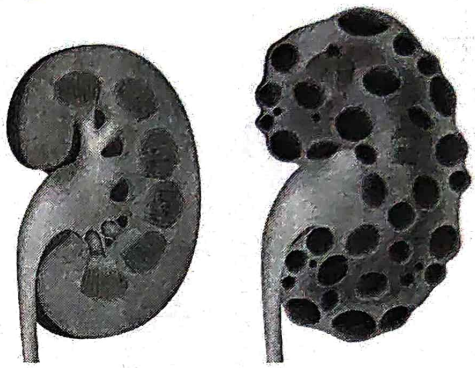
- Most common monogenic kidney disease 1 in 1000
- Genetics AD

PKD1 gene chromosome 16 → Polycystin 1

PKD2 gene chromosome 4 → Polycystin 2

Growth Factors ↑

mTOR



Renomegaly (dt multiple cyst - larger cyst)

cortex > medulla.

CMD lost

CLINICAL FEATURES

- Age 3rd to 4th decade.

✓ Pain - cyst infection (palpable renal mass)
cyst rapture, stretching of cyst

✓ Hematuria

✓ Renal infection ↑ risk of UTI

✓ Hypertension ↑ activation of RAAS
↑ risk of renal calculi

Extra-renal manifestations

initially RFT - (N)

↓

Renal ~~replacement~~ impairment

↓

Renal failure.

Hepatic cyst, splenic cyst, pancreatic cyst, seminal vesicle cyst, colonic diverticula, berry aneurysm, MVP

INVESTIGATIONS

- USG abdomen, CT / MRI abdomen

TREATMENT

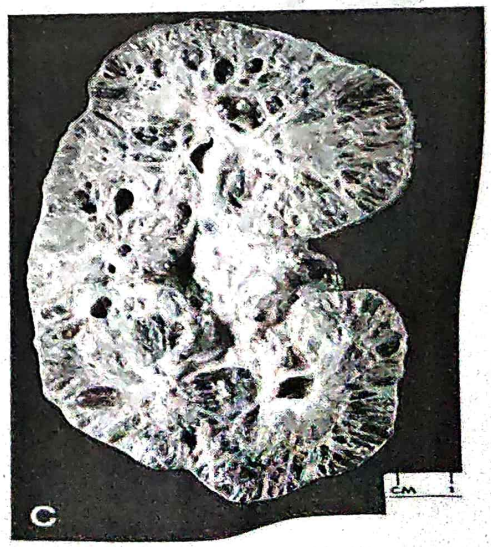
- ACEI/ARB → Decrease proteinuria, control BP
- Vasopressin antagonists → Tolvaptan
- Somatostatin analogues – octreotide
- Inhibitors of cell proliferation – mTOR inhibitors
  Sirolimus, Everolimus

↳ RRT

ARPKD

- Hereditary renal disease in childhood
- Genetics AR.

PKHD1 - mutation
– coding for fibrocystin
Chr. 6
↳ Renomegaly,
smaller cyst
medulla > cortex
linear striations
in cortex



CLINICAL FEATURES

- Perinatal, Neonatal, Infantile, Juvenile

↓

oligohydraminosis — early renal impairment
pulmonary hypoplasia

INVESTIGATIONS

USG, CT, MRI

TREATMENT

Supportive

MEDULLARY SPONGE KIDNEY

- Disease involving distal nephron → CCD, MCD (medullary collecting duct)
- Age group 4th–5th decade

↓

Sponge like appearance

CLINICAL FEATURES

Most common clinical presentation – Nephrolithiasis

Hematuria

Recurrent UTI

Investigation → IVP, CTU

↓

Paint Brush appearance

TREATMENT

~~Bourdeti~~ ACEI/ ARB.

TUBEROUS SCLEROSIS

- Bourneville's disease

- Genetics

TSC1 — chr. 9 hamartin

TSC2 — chr 16 Tuberin.

mTOR ↑

CLINICAL FEATURES

- Kidney – Renal angiomyolipoma (m.c), Renal cysts, Renal cell carcinoma

– Wunderlich syndrome Flank pain, Flank mass, Hypotension

- Skin
  – Ash leaf macules, Adenoma sebaceum, Shagreen patches, Koenen tumors

Gpl LoIA - adenosphebaceum } vogt's triad
↓ ↳ low Iq
epilepsy

→ seplepsy

- CNS SEGCA
  Subependymal grant cell astrocytoma
  perirentricular · "Tubers"
- Heart → Rhabdomyoma.

I.O.C - Genetic analysis

TREATMENT

Supportive
mTOR inhibitors
RRT

VON HIPPEL LINDAU SYNDROME

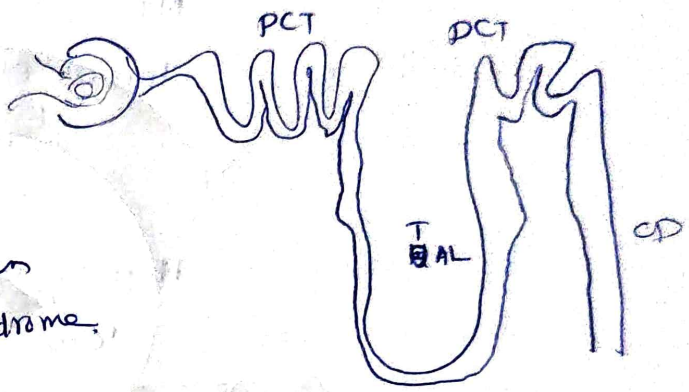
- Genetics → chromosome 3.
  VHL
- Renal manifestations Renal cysts, RCC
- Non-renal manifestations
  - Pheochromocytomas, Cerebellar hemangioblastomas, Retinal hemangiomas, Endolymphatic sac tumors

I.O.C
Genetic analysis

Rx
Supportive

INHERITED TUBULAR DISORDERS OF ELECTROLYTE HANDLING

- Bartter syndrome, Gitelman syndrome, Liddle syndrome



② Na^+Cl^- symport.

location: DCT

gene: SLC12A3

Gain of function – Gordan mutation

loss of function – Gitelman syndrome

loss of Na^+, Cl^-, in urine – low BP.

RAAS activation – met. alkalosis

Gordan is mirror image of Gitelman

℞ K+ supplements

supportive.

① $Na^+K^+2Cl^-$ – location

TAL of Loop of Henle

Gene – SLC12A1

gain of function mutation

Bartter syndrome ← loss of function mutation

- ↓ Urinary loss of Na^+, K^+, Cl^-
- ↓ Hypovoluemia, low BP
- ↑ stimulation of RAAS – metabolic alkalosis

5 types ① Na^+, K^+, $2Cl^-$. ④ Bartin – deafness gene

③ ENaC

Epithelial Na channel

℞ Indomethacin

Gain of function – Liddle

loss of function – Pseudoaldosteronism type.

Liddle → High BP

metabolic acidosis

℞ : Amiloride.

FEATURE	BARTTER	GITELMAN	LIDDLE
Inheritance	AR	AR	D
Affected tubule	TAL - LH	DCT	P cell of CD
Ion channel	$Na^+ K^+ 2Cl^-$	$Na^+ Cl^-$	ENaC
Electrolyte imbalance	loss of Na^+, K^+, Cl^-, H^+	loss of Na^+, Ca^+, Cl^-, H^+	Retension of Na^+, loss of K^+, H^+
Urinary calcium	High Urinary Ca^-	low	Normal
Blood pressure	low	low	high
	Indomethacin	Ca^+ supplements	Amiloride

RENAL TUBULAR ACIDOSIS

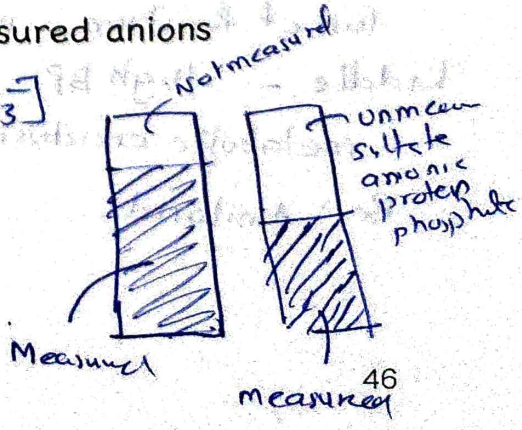
- Metabolic acidosis + Defective renal tubular function
- Normal/near normal GFR

ANION GAP

- Serum anion gap = Measured cations - Measured anions

$$Na^+ - [Cl^- + HCO_3^-]$$

8-12 meq/L
average - 10 meq/L



Metabolic acidosis

↙ High anion GAP metabolic acidosis

↘ NAGMA

- Corrected anion gap = Observed AG + 2.5 (4.5 - measured albumin)
- HAGMA

Causes - Lactic acidosis, Ketoacidosis, Toxins, Renal failure

↪ ethyleneglycol, methanol

Ketoacidosis

↙ Alcoholic ketoacidosis ↓ starvation K.A

↘ Diabetic acidosis

Acid

↙ Ht

↘ Acid anion.

- Osmolal gap = Measured osmolality - Calculated osmolality

Hyperchloremic metabolic acidosis

- NAGMA → Normal / Non anion gap metabolic acidosis

Renal causes – Renal tubular acidosis +ve UAG

-ve UAG.

Extra-renal causes – Diarrhea, urinary diversion procedure. (Ureterosigmoidostomy)

↓

loss of bicarbonate.

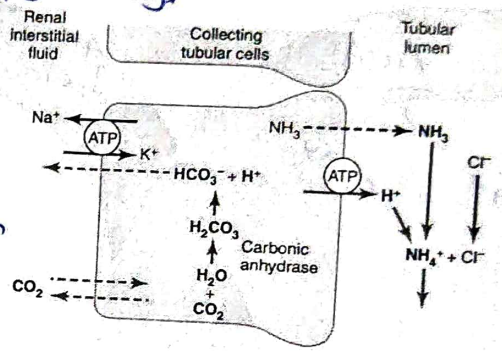
NAGMA

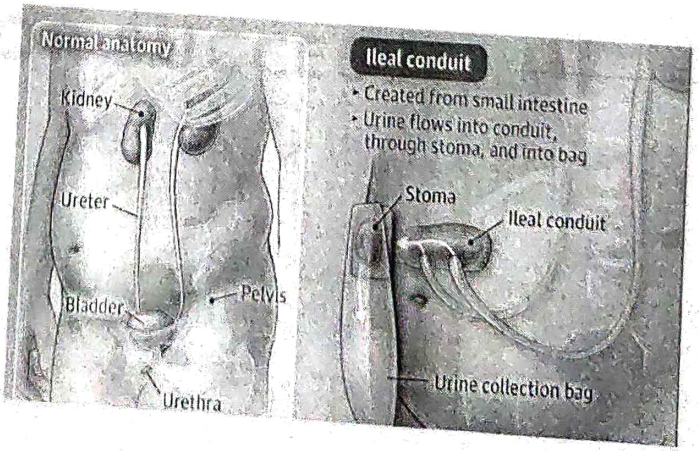
Renal response acidification ⊕

Diarrhea

Renal acidification response ⊖

RTA





- Urine anion gap

$[Na^+ + K^+] - [Cl^-]$

Negative urinary anion gap (Diarrhea)

Positive urinary anion gap (RTA)

- Urine osmolal gap 50 – 1200 mosmol/kg

Measured urine osmolality – calculated urine osmolality

Osmometer.

Na^+, RBS, BUN, NH_4^+

Na^+, RBS BUN

>100 mosmol/kg → Diarrhea

<100 mosmol/kg → RTA

classic – RTA Urine pH – 4–8

Type I RTA → α intercalated cells – DCT, CCD.

- Inability to excrete H+ by distal nephron – H^+ acidosis
- Urine pH > 5.5 despite systemic acidosis
- Metabolic acidosis – reabsorption of bone matrix → ↑↑ serum Na^+
- Increased urinary calcium excretion
- Nephrolithiasis, Nephrocalcinosis
- Positive urine anion gap
- Hypokalemia

C/f - weakness
- Nephrolithiasis
- Nephrocalcinosis
- Nephrogenic diabetic insipidus

- Causes - Sjogren syndrome, Amphotericin B, Lithium
- Treatment - alkali supplementation

Type II RTA

- Defect in bicarbonate reabsorption Bicarbonaturia.
  Generalised PCT dysfunction.
- Urine pH <5.5 (dlt preserved function of α-intercalated cells)
- Fanconi syndrome - glucosuria, aminoaciduria, phosphaturia, uricosuria,
- Causes - Multiple myeloma, Cystinosis, Acetazolamide Citraturia
  Wilson disease.

  No nephrolithiasis
  - Hypokalemia
- Treatment Alkali supplimentation.

Type IV RTA

Type III - Type I + Type II feature of

- Generalized distal nephron dysfunction → CCD + MCD

- Most common RTA in clinical practice
- Causes - Diabetic nephropathy, Tubulointerstitial renal diseases ↓ renin
- Hyporeninemic hypoaldosteronism ACE I / ARB
  - Hyperkalemia.

- Treatment

  Alkali supplementation.

TUTORIALS
LOGIN FOR SUCCESS