Glomerulonephritis

- Third commonest cause of ESKD
  – 10-15%
  (after DM & HPT)

- Group of disorders with,
  - Immunologically mediated glomerular injury
  - Both kidneys equally affected
  - May be part of generalized disease
    eg - SLE

Pathogenesis

- Immune complexes deposition/in-situ formation
- Anti-glomerular basement membrane antibody (Anti-GBM Ab) deposition
- Atypical immunoglobulin deposition
  eg - IgA

Classification

- No complete correlation between histological types of GN and clinical features of disease
- Easy classification – based on 4 major glomerular syndromes

Classification

- Nephrotic syndrome
- Acute glomerulonephritis (acute nephritic syndrome)
- Rapidly progressive glomerulonephritis (RPGN)
- Asymptomatic haematuria, proteinuria or both

Acute Glomerulonephritis (AGN)

- Sudden onset of glomerular haematuria
  (dysmorphic RBC, RBC casts)
- Proteinuria
  (non-nephrotic range)
- Oedema
- Hypertension
- Transient renal impairment

Rapidly Progressive Glomerulonephritis (RPGN)

- Features of acute nephritis
- Renal biopsy → focal necrosis +/- crescents
- Rapidly progressive renal failure (over weeks)

Asymptomatic Urinary Abnormalities

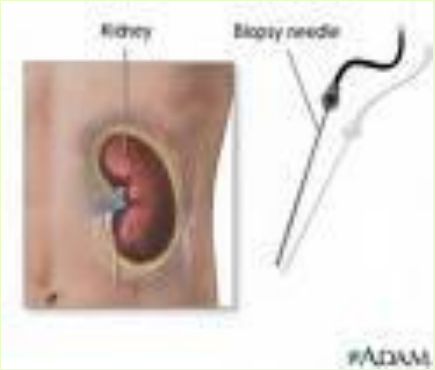
- IgA Nephropathy
- Alports syndrome with deafness, X-linked

Investigation of Glomerular Disease

Investigations	Positive findings
Urine microscopy	Red cells, red-cell casts
Urinary protein	Nephrotic or sub-nephrotic range proteinuria
Serum urea	May be elevated
Serum creatinine	May be elevated
Culture (throat swab, discharge from ear, swab from inflamed skin)	Nephritogenic organism (not always)
Antistreptolysin-O titre	Elevated in post-streptococcal nephritis
C3 and C4 levels	May be reduced
Antinuclear antibody	Present in significant titre in systemic lupus erythematosus
ANCA	Positive in vasculitis
Anti-GBM	Positive in Goodpasture's syndrome
Cryoglobulins	Increased in cryoglobulinaemia
Creatinine clearance	Normal or reduced
Chest X-ray	Cardiomegaly, pulmonary oedema (not always)
Renal imaging	Usually normal
Renal biopsy	Any glomerulopathy

Renal Biopsy in Diagnosing GN

- Uncertain diagnosis
- Unusual clinical features
- Rapidly progressing renal failure



Not indicated *if clinical diagnosis of nephritic illness is clear-cut*

Acute Glomerulonephritis (AGN)

- **Syndrome of –**

  macro/microscopic haematuria +/- RBC casts
  proteinuria
  hypertension
  oedema - periorbital, leg, sacral
  temporary oliguria & uraemia

- **Histology –**

  mesangial & endothelial cellular proliferation
  inflammatory cell infiltration

Association with AGN

- Post-streptococcal GN
- Post-infectious GN –
  staph, HBV
- Infective Endocarditis
- SLE
- HSP

Post-Streptococcal GN (PSGN)

- Patient usually a child
- Streptococcal infection 1-3 weeks before
  (tonsillitis, pharyngitis, otitis media, cellulitis)
- Lancefield Group A ß haemolytic streptococcus of nephritogenic type

Management of PSGN

- Anti-hypertensives
- Diuretics
- Salt restriction
- Dialysis SOS
- Penicillin to eradicate infection
- Corticosteroids if recovery is slow

Complications of PSGN

- Hypertensive encephalopathy
  - maintain airway
  - iv antihypertensives (sodium nitroprusside, hydralazine)
  - iv Diazepam for fits
- Pulmonary oedema
  - high dose iv Furosemide, O2 via mask
  - dialysis
- Severe uraemia
  - dialysis

Prognosis of PSGN

- Good in children
- In a few adults later in life – HPT & renal impairment

  Need annual BP & s.creatinine check

Mixed Nephritic / Nephrotic GN

Primary

- Mesangio-capillary GN
- Mesangial proliferative GN

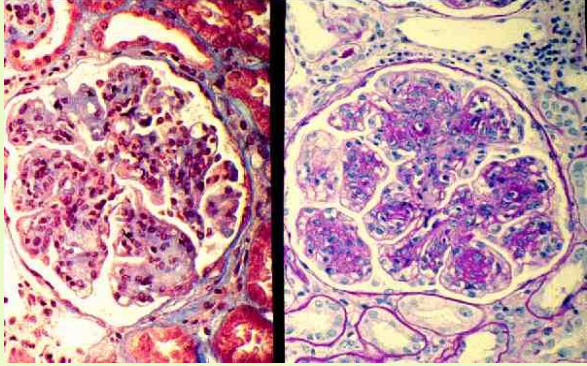
Secondary

- SLE
- HSP
- Cryoglobulinaemic disease
- Idiopathic fibrillary & Immunotactoid GN

Mesangiocapillary GN (MCGN)

- Rare
- 3 subtypes
- All present with NS, HPT, haematuria, renal impairment
- Similar LM, defined by EM appearance

Type I MCGN



- 'Tram line' effect – split basement membrane
- ↓ C3 & normal C4 (classical complement pathway)

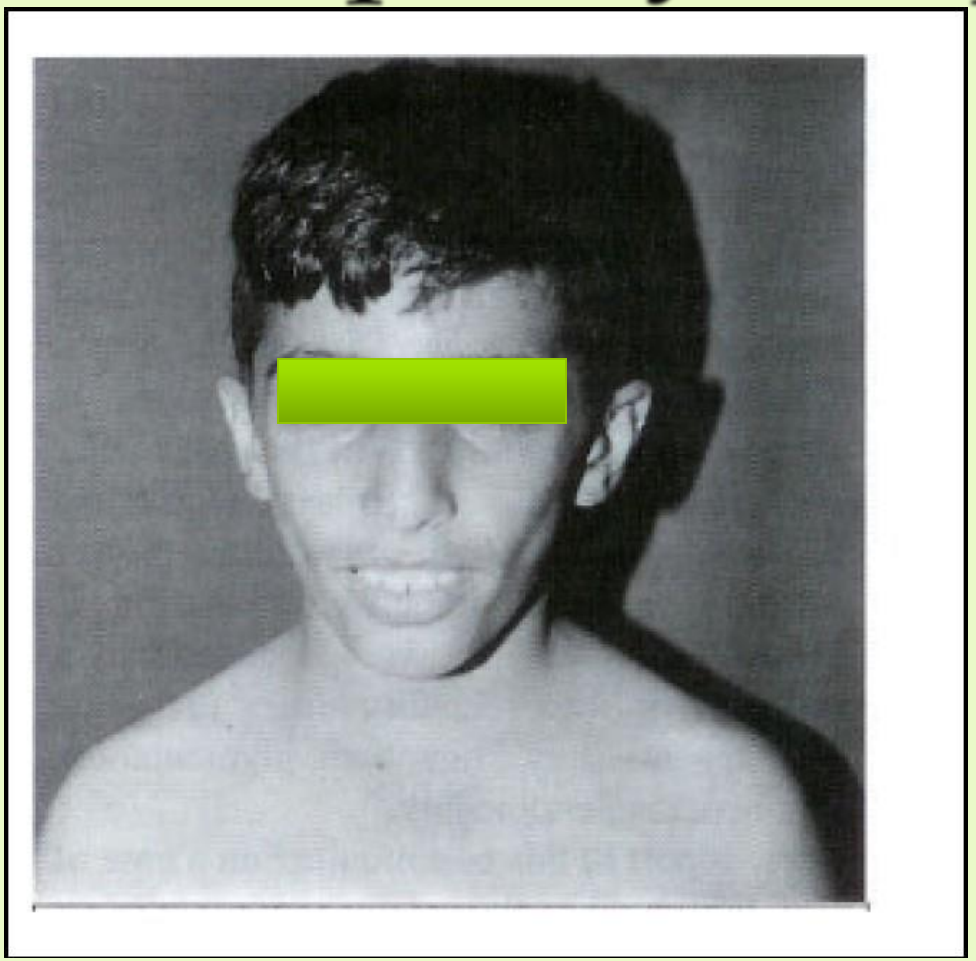
- Idiopathic
- With chronic infection – abscess, IE, VP shunt infections
- With cryoglobulinaemia secondary to HCV

Type II MCGN

- Intra-membranous C3 deposits
- ↓ C3 (alternate complement pathway)
- Auto Abs to C3 convertase

- Young adults
- Idiopathic or associated with partial lipo-dystrophy
- Recurs in transplants but does not interfere with graft function

Partial Lipo-dystrophy



Type III MCGN

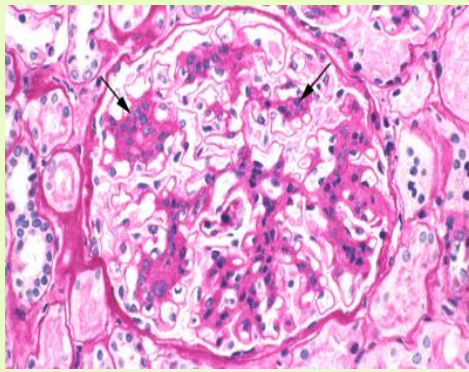
- Features of Types I & II
- Complement activated via final common pathway

- *Most with MCGN develop CKD over years*

MCGN - Treatment

- If normal renal function + mild proteinuria → follow up only, control BP
- If nephritic/renal impairment →
  Aspirin &/or Dipyridamole for 6-12 months
  (prednisolone for children)

Mesangial Proliferative GN



IgM Nephropathy

- IgM & complement deposits
- NS + haematuria
- 50% respond to steroids
- 10-30% progressive renal failure (secondary FSGS)
- cyclophosphamide + steroids if NS with rising creatinine

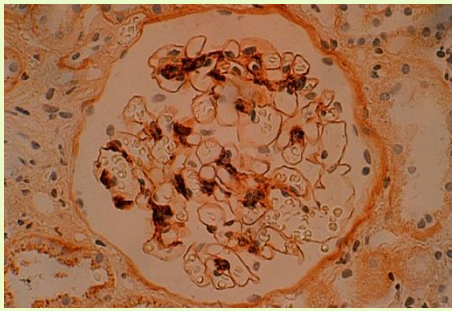
Mesangial Proliferative GN

C1q Nephropathy

- C1q deposits - similar to IgM
- mistaken for lupus nephritis
- NS + haematuria
- some steroid dependent
- may progress to CKD

Asymptomatic Urinary Abnormalities

IgA Nephropathy



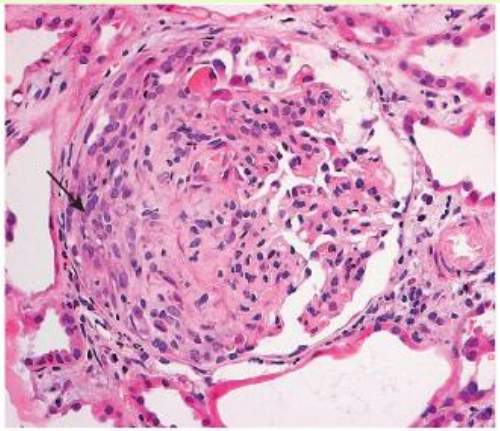
- commonest GN worldwide
- Histo – focal & segmental proliferative GN with mesangial deposits of IgA
- children & young males
- asymptomatic microscopic haematuria or recurrent macroscopic haematuria preceeding upper resp/GI viral infection +/- proteinuria

IgA Nephropathy - Management

- Good prognosis if normal BP, normal renal function & no proteinuria
- Some may develop CKD
- Tonsillectomy
- Steroids
- Fish oil
- Cyclophosphamide
- ACEI + ARB

Rapidly Progressive Glomerulonephritis (RPGN) - Types

- Goodpastures syndrome (anti-GBM Ab)
- Idiopathic
- Associated with other primary / secondary GN
- ANCA-associated vasculitis syndromes



(b)

Anti-GBM Glomerulonephritis

- Rare

- Associated lung haemorrhages (Goodpastures syndrome)
- Renal restricted

- Plasma exchange
- Steroids
- Cyclophosphamide

- May lead to ESKD
-

Fig. 1 : X-ray chest : Bilateral fluffy shadows.

ANCA-positive Vasculitides

- Small vessel vasculitis due to anti-neutrophil cytoplasm antibodies

- **Wegener's granulomatosis**
  Microscopic polyangiitis
  Churg-Strauss syndrome

- Multi-system diseases – skin, lungs, joints, fever, malaise

- High dose steroids
- Cyclophosphamide
- Plasma exchange

- May lead to ESKD

Summary

- GN= immunological inflammation in glomeruli
- Classification based on histology
- Different diseases – same histology
  Same disease – different histologies
- Clinical spectrum ranges from acute to chronic
  4 main clinical presentations – each managed differently
- Acute nephritic syndrome – prototype is Post-streptococcal GN
- RPGN is a renal emergency