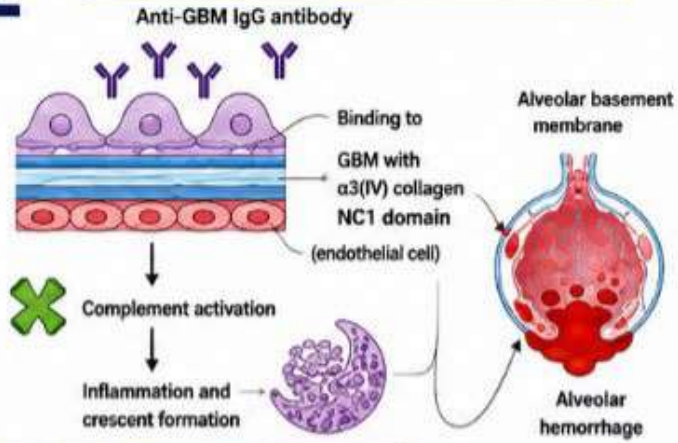
ANTI-GBM DISEASE
(Goodpasture Syndrome)

A rare autoimmune disease caused by antibodies against the non-collagenous (NC1) domain of the α3 chain of type IV collagen in the glomerular and alveolar basement membranes.

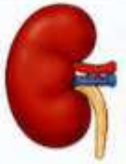
Causes rapidly progressive glomerulonephritis ± pulmonary hemorrhage (Goodpasture syndrome).

PATHOGENESIS



CLINICAL FEATURES

RENAL



- Hematuria (microscopic/gross)
- Proteinuria (nephrotic range)
- Rapid rise in serum creatinine
- Hypertension
- Oliguria / anuria

PULMONARY

- Hemoptysis
- Dyspnea, cough
- Diffuse alveolar infiltrates
- Respiratory failure

Goodpasture syndrome = Anti-GBM disease ± pulmonary hemorrhage

TRIGGERS / ASSOCIATIONS


Smoking


Respiratory infections


Hydrocarbon exposure


Cocaine inhalation


Genetic predisposition (HLA-DR15)

DIAGNOSIS

Laboratory

- Anti-GBM antibody (ELISA) positive in 70–90%
- Urinalysis:
  - Dysmorphic RBCs
  - RBC casts
  - Mild to moderate proteinuria
- Serum creatinine

Kidney Biopsy (Gold Standard)


Light microscopy: Diffuse crescentic glomerulonephritis


Immunofluorescence: Linear IgG staining along the GBM (± C3 and κ)


Electron microscopy: No immune-complex deposits

DIFFERENTIAL DIAGNOSIS

DISEASE	IMMUNOFLUORESCENCE PATTERN
Anti-GBM disease	Linear IgG
ANCA vasculitis	Pauci-immune (negative or minimal)
Lupus nephritis	Granular ("full house")
IgA nephropathy	Mesangial IgA

ANCA ASSOCIATION

- 30–40% of patients are ANCA positive (usually MPO-ANCA).
- Dual-positive patients have apparent SLE or ANCA disease before the ANCA vasculitis, and have a higher relapse risk than isolated anti-GBM disease.

TREATMENT (Start early – do not wait for biopsy if strongly suspected)

1. PLASMA EXCHANGE (PLEX)

- Daily or alternate-day sessions
- Continue for 10–14 days or until antibodies undetectable
- Removes circulating anti-GBM antibodies

2. CORTICOSTEROIDS

- IV methylprednisolone 500–1000 mg/day for 3 days
- Followed by oral prednisone 1 mg/kg/day, then gradual taper

3. CYCLOPHOSPHAMIDE

- Oral 2 mg/kg/day or IV pulse regimen
- Suppresses new antibody formation

KDIGO 2024–2025 APPROACH

Treat with:

- Plasma exchange
- High-dose glucocorticoids
- Cyclophosphamide

Kidney transplantation should be delayed until anti-GBM antibodies have remained negative for at least 6 months.

PROGNOSIS

Poor prognosis if:

- Serum creatinine >5–6 mg/dL
- Severe alveolar hemorrhage
- >50% crescents on biopsy
- Treatment delay >2 weeks

Better prognosis if:

- Diagnosed early
- Serum creatinine <5 mg/dL
- Limited crescent formation
- Prompt initiation of plasma exchange

Relapse occurs 10–25%. Risk reduces after 6–12 months of sustained immunosuppression.

Recurrence post-HCT/Tx is lower in anti-GBM disease, higher in dual-positive MPO (+) anti-GBM.

TARGET ANTIGEN NC1 domain of the α3 chain of type IV collagen

KEY POINTS Autoantibody to GBM (α3(IV) NC1) • Linear IgG on IF • Rapidly progressive GN ± pulmonary hemorrhage • Treat early: PLEX + Steroids + Cyclophosphamide

ECNG

Extracorporeal Nephrology Group

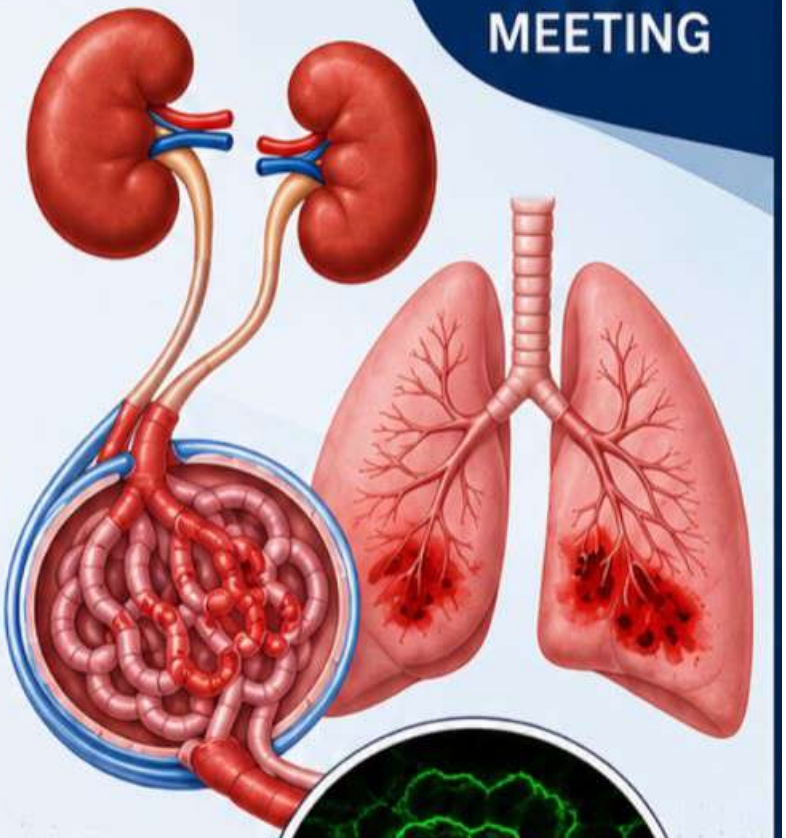
An Academic Forum for Nephrologists, Dialysis Trainers, Physicians, and Healthcare Professionals

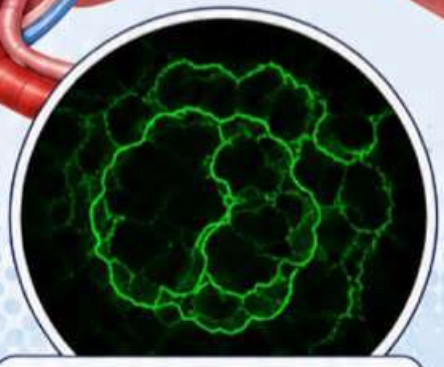
LIVE ZOOM MEETING

Anti-GBM Disease

(Goodpasture Syndrome)

Pathogenesis • Clinical Features • Diagnosis
Treatment • Prognosis





Classic linear IgG deposition along the glomerular basement membrane (GBM)

KEY HIGHLIGHTS

- Anti-GBM antibodies & disease pathogenesis
- Renal manifestations
- Pulmonary hemorrhage (Goodpasture syndrome)
- Diagnosis: Serology, Kidney biopsy & Immunofluorescence
- Treatment: Plasma Exchange (PLEX), Corticosteroids & Cyclophosphamide
- Prognosis and long-term outcomes

ANTI-GBM DISEASE

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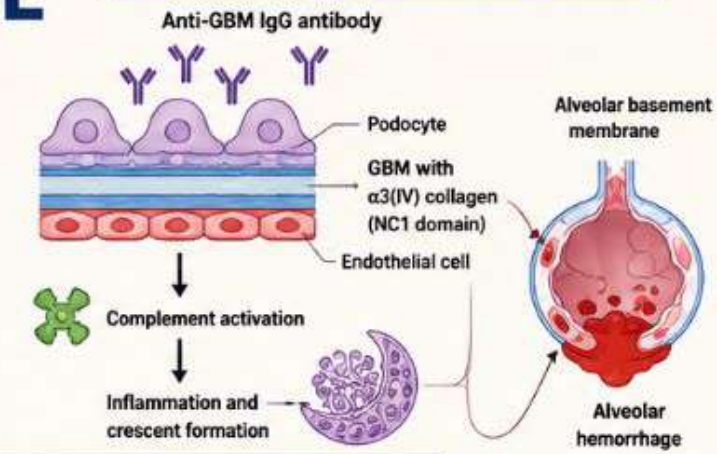

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- Dual-positive patients may present like anti-GBM disease, behave like ANCA vasculitis, and have a higher relapse risk than isolated anti-GBM disease.

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- Plasma exchange
- High-dose glucocorticoids
- Cyclophosphamide

Kidney transplantation should be delayed until anti-GBM antibodies have remained negative for at least 6 months.

PROGNOSIS

Poor prognosis if:

- Serum creatinine >5–6 mg/dL
- Dialysis dependence at presentation
- 100% crescents on biopsy
- Severe oliguria/anuria

Better prognosis if:

- Diagnosed early
- Serum creatinine <5 mg/dL
- Limited crescent formation
- Prompt initiation of plasma exchange

Patient survival >80–90% with modern therapy

Renal survival depends on kidney function at presentation

Relapse uncommon (<5%) in isolated anti-GBM disease; higher in dual-positive (ANCA + anti-GBM).

TARGET ANTIGEN NC1 domain of the α3 chain of type IV collagen

KEY POINTS Autoantibody to GBM (α3(IV) NC1) • Linear IgG on IF • Rapidly progressive GN ± pulmonary hemorrhage • Treat early: PLEX + Steroids + Cyclophosphamide

DIFFERENTIAL DIAGNOSIS OF GOOD PASTURE'S SYNDROME (ANTI-GBM DISEASE)

CONDITION	KEY FEATURES	AUTOANTIBODY / SEROLOGY	RENAL FINDINGS	PULMONARY FINDINGS	CLUES THAT FAVOR THE CONDITION
GOOD PASTURE'S SYNDROME (ANTI-GBM DISEASE)	• Rapidly progressive glomerulonephritis • Pulmonary hemorrhage • Young adults (male > female) • No extrarenal involvement	Anti-GBM antibody (Linear IgG staining along GBM) Positive	• RPGN • Linear IgG staining along GBM • No immune complex deposition	• Diffuse alveolar hemorrhage • Hemoptysis • Anemia	Positive anti-GBM antibody with linear IgG staining along GBM
ANCA-ASSOCIATED VASCULITIS (GRANULOMATOSIS WITH POLYANGIITIS)	• RPGN • Pulmonary hemorrhage • Upper & lower respiratory tract involvement • Systemic features (fever, weight loss, ENT involvement)	c-ANCA (PR3-ANCA) usually positive p-ANCA (MPO-ANCA) may be positive	• Pauci-immune RPGN • No linear IgG staining	• Nodules, cavities • DAH possible • Sinusitis, otitis media common	ENT involvement, c-ANCA positivity, granulomatous inflammation
MICROSCOPIC POLYANGIITIS	• RPGN • Pulmonary hemorrhage • Systemic features • No granulomas • No ENT involvement	p-ANCA (MPO-ANCA) positive	• Pauci-immune RPGN • No linear IgG staining	• DAH possible • No nodules or cavities	p-ANCA positivity, absence of ENT disease and granulomas
SYSTEMIC LUPUS ERYTHEMATOSUS (LUPUS NEPHRITIS)	• RPGN (Class IV) • Pulmonary hemorrhage (uncommon) • Rash, arthritis, serositis • Hypocomplementemia	ANA + Anti-dsDNA + (Variable)	Immune complex GN • "Full house" immunofluorescence (IgG, IgA, IgM, C3, C1q)	• Pleuritis common • DAH uncommon	ANA, anti-dsDNA positivity, low C3/C4, other SLE features
IMMUNE COMPLEX GLOMERULONEPHRITIS (POST-INFECTIOUS / (GA NEPHROPATHY)	• Hematuria (often macroscopic) • Edema, hypertension • Recent infection (Post-infectious) • Hearing loss (post-streptococcal)	No specific antibody (ASO ↑ in post-streptococcal GN)	• Immune complex GN • Granular Ig and C3 deposition	• Pulmonary hemorrhage rare	Recent infection, low C3, granular immune deposits
DRUG-INDUCED PULMONARY-RENAL SYNDROME	• RPGN • Pulmonary hemorrhage • Drug exposure (history crucial)	ANCA may be positive or negative	• Pauci-immune or immune complex GN	• DAH possible	Recent exposure to drugs (e.g., Hydralazine, Propylthiouracil, Penicillamine, Cocaine, etc.)
ANTI-PLA2R ASSOCIATED MEMBRANOUS NEPHROPATHY	• Nephrotic syndrome • Hematuria mild or absent • No pulmonary hemorrhage	Anti-PLA2R antibody positive	• Subepithelial immune deposits (spike & dome pattern) • No RPGN	• No pulmonary involvement	Nephrotic range proteinuria, anti-PLA2R positive, no lung disease

KEY POINT

The hallmark of Good Pasture's Syndrome is the presence of anti-GBM antibodies with linear IgG staining along the GBM and pulmonary hemorrhage with rapidly progressive GN, without systemic vasculitis features.

RPGN – Rapidly Progressive Glomerulonephritis
DAH – Diffuse Alveolar Hemorrhage
GBM – Glomerular Basement Membrane
ANCA – Anti-Neutrophil Cytoplasmic Antibody
ANA – Antinuclear Antibody

Careful history, serology, and renal biopsy with immunofluorescence are key to accurate diagnosis and appropriate therapy.