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# History in Nephrology

*True Legends are immortal through their deeds and memories.!*

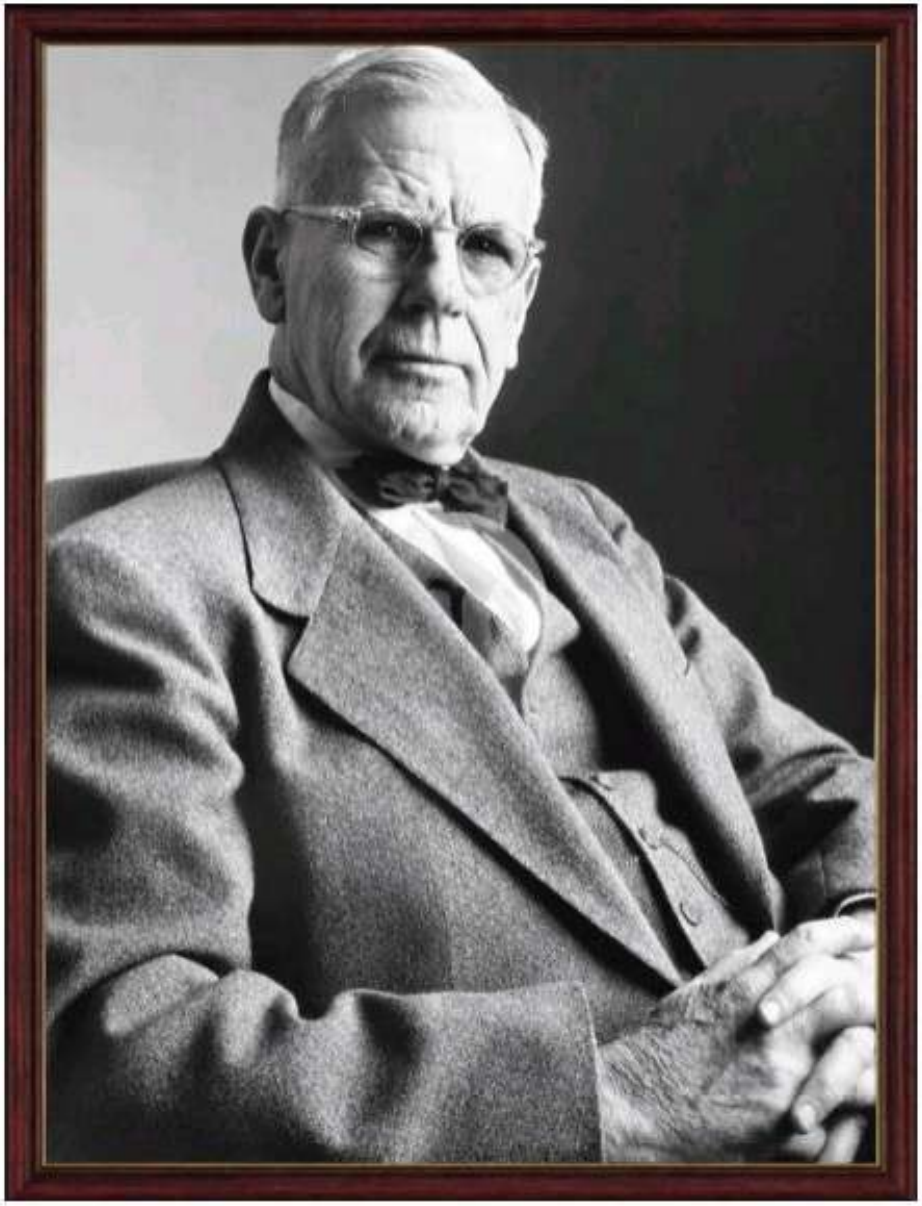
## Anti – GBM Disease
## (Goodpasture Syndrome)

**Dr. Ernest William Goodpasture**

**Dr. Robert A Lerner**

**Dr. Curtis B Willson**

**Dr. John Dixon**



# Dr. Ernest William Goodpasture

- Described the syndrome in 1919.
- Reported a young man with pulmonary haemorrhage and rapidly progressive glomerulonephritis during the influenza pandemic.
- This condition was later named Goodpasture syndrome in his honor

Robert A. Lerner

Curtis B. Wilson

John Dixon

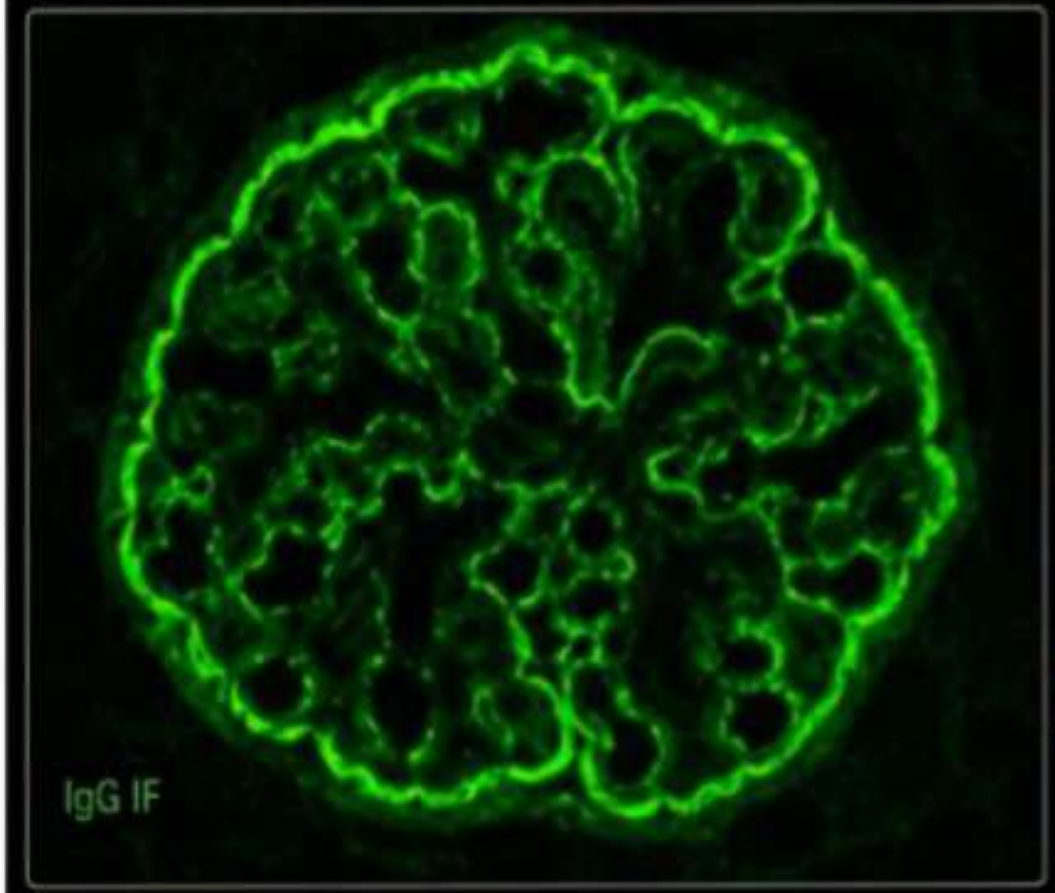
In 1967, Robert A. Lerner, Curtis B. Wilson and John Dixon demonstrated that the disease is caused by circulating antibodies directed against the glomerular basement membrane (GBM).

Late 1980s: Target antigen identified as the a3(IV) collagen NC1 domain

# Immunofluorescence (IF) Study

## Glomerulus in Anti-GBM Disease (Goodpasture's Syndrome)

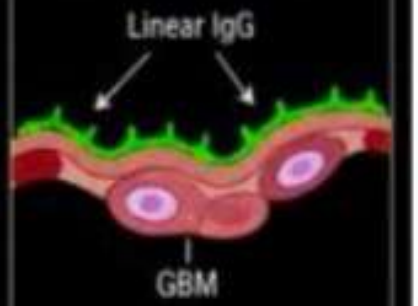
*Linear IgG Deposition Along Glomerular Basement Membrane (GBM)*




**FINDING**

- Strong, smooth, linear IgG staining along glomerular capillary basement membranes
- No significant staining in mesangium

**SCHEMATIC DIAGRAM**




**INTERPRETATION**

Linear IgG deposition along GBM is characteristic of Anti-GBM disease (Goodpasture's Syndrome) and helps differentiate it from immune complex–mediated glomerulonephritides, which show granular staining.

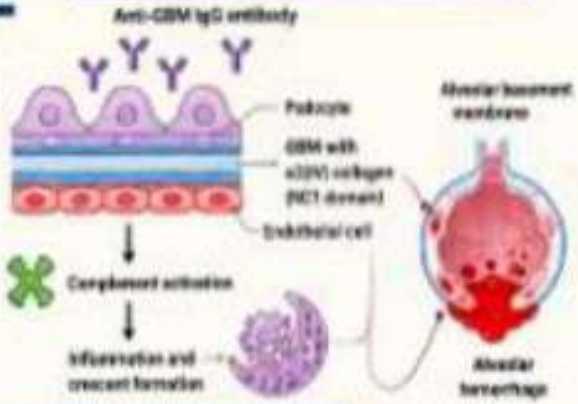
# ANTI-GBM DISEASE

## (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 90–95%
- 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 (hallmark)

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 may present like anti-GBM 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

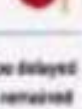
### 3. CYCLOPHOSPHAMIDE

- 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:**

- Severe creatinine >5–6 mg/dL
- Dialysis dependence at presentation
- >50% crescents on biopsy
- Severe oligoanuria

**Better prognosis if:**

- Diagnosed early
- Serum creatinine <3 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 common (~25%) 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<br>• Pulmonary hemorrhage<br>• Young adults (male > female)<br>• No extrarenal involvement | Anti-GBM antibody (Linear IgG staining along GBM)<br>Positive | • RPGN<br>• Linear IgG staining along GBM<br>• No immune complex deposition | • Diffuse alveolar hemorrhage<br>• Hemoptysis<br>• Anemia | Positive anti-GBM antibody with linear IgG staining along GBM |
| **ANCA-ASSOCIATED VASCULITIS (GRANULOMATOSIS WITH POLYANGIITIS)** | • RPGN<br>• Pulmonary hemorrhage<br>• Upper & lower respiratory tract involvement<br>• Systemic features (Fever, weight loss, ENT involvement) | c-ANCA (PR3-ANCA) usually positive<br>p-ANCA (MPO-ANCA) may be positive | • Pauci-immune RPGN<br>• No linear IgG staining | • Nodules, cavities<br>• DAH possible<br>• Sinusitis, otitis media common | ENT involvement, c-ANCA positivity, granulomatous inflammation |
| **MICROSCOPIC POLYANGIITIS** | • RPGN<br>• Pulmonary hemorrhage<br>• Systemic features<br>• No granulomas<br>• No ENT involvement | p-ANCA (MPO-ANCA) positive | • Pauci-immune RPGN<br>• No linear IgG staining | • DAH possible<br>• No nodules or cavities | p-ANCA positivity, absence of ENT disease and granulomas |
| **SYSTEMIC LUPUS ERYTHEMATOSUS (LUPUS NEPHRITIS)** | • RPGN (Class IV)<br>• Pulmonary hemorrhage (uncommon)<br>• Rash, arthritis, serositis<br>• Hypocomplementemia | ANA +<br>Anti-dsDNA +<br>(Variable) | • Immune complex GN<br>• "Full house" immunofluorescence (IgG, IgA, IgM, C3, C1q) | • Pleuritis common<br>• DAH uncommon | ANA, anti-dsDNA positivity, low C3/C4, other SLE features |
| **IMMUNE COMPLEX GLOMERULONEPHRITIS (POST-INFECTIOUS / IGA NEPHROPATHY)** | • Hematuria (often macroscopic)<br>• Edema, hypertension<br>• Recent infection (Post-infectious)<br>• Hearing loss (post-streptococcal) | No specific antibody (ASO ↑ in post-streptococcal GN) | • Immune complex GN<br>• Granular Ig and C3 deposition | • Pulmonary hemorrhage rare | Recent infection, low C3, granular immune deposits |
| **DRUG-INDUCED PULMONARY-RENAL SYNDROME** | • RPGN<br>• Pulmonary hemorrhage<br>• 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<br>• Hematuria mild or absent<br>• No pulmonary hemorrhage | Anti-PLA2R antibody positive | • Subepithelial immune deposits (spike & dome pattern)<br>• 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.