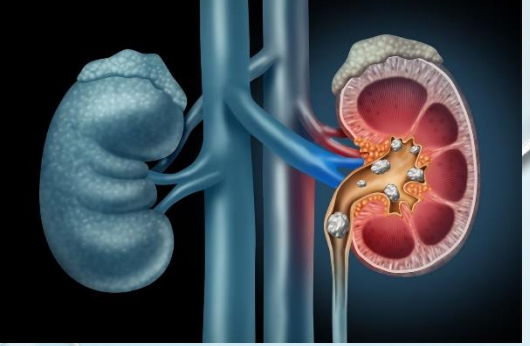


# ANTI-GBM ANTIBODY DISEASE

**DR AKSHAY KULKARNI**

**RESIDENT, DEPT. OF NEPHROLOGY**

**DR D.Y PATIL MEDICAL COLLEGE,HOSPITAL AND RESEARCH CENTRE, PUNE**

# CASE SCENARIO

- 34 years old lady
- Reduced urination, swelling over feet and face- 8 days
- Hematuria- 4 days
- Hypertension- 2 years on T. Telmisartan 40 mg OD

# CASE SCENARIO

- Vitals : pulse 98/ min, BP 160/90 mmHg
- Bilateral pitting pedal edema +
- Pallor +
- Urine routine- protein 2+, RBC 80-90/hpf, pus cells 3-4/hpf

# LAB REPORTS

- Hb 7.8, TLC 8100, Platelet 169000
- Urea 203, Creat 13.08, Na 135, K >6
- Sr. total protein 5.7 mg/dl, albumin 3.5mg/dl
- UPCR- 7.5 mg/mg
- HbA1c- 6 %
- USG A/P: RK 104x37mm, LK 99x32mm, bilateral raised echogenicity

# DIAGNOSIS ?

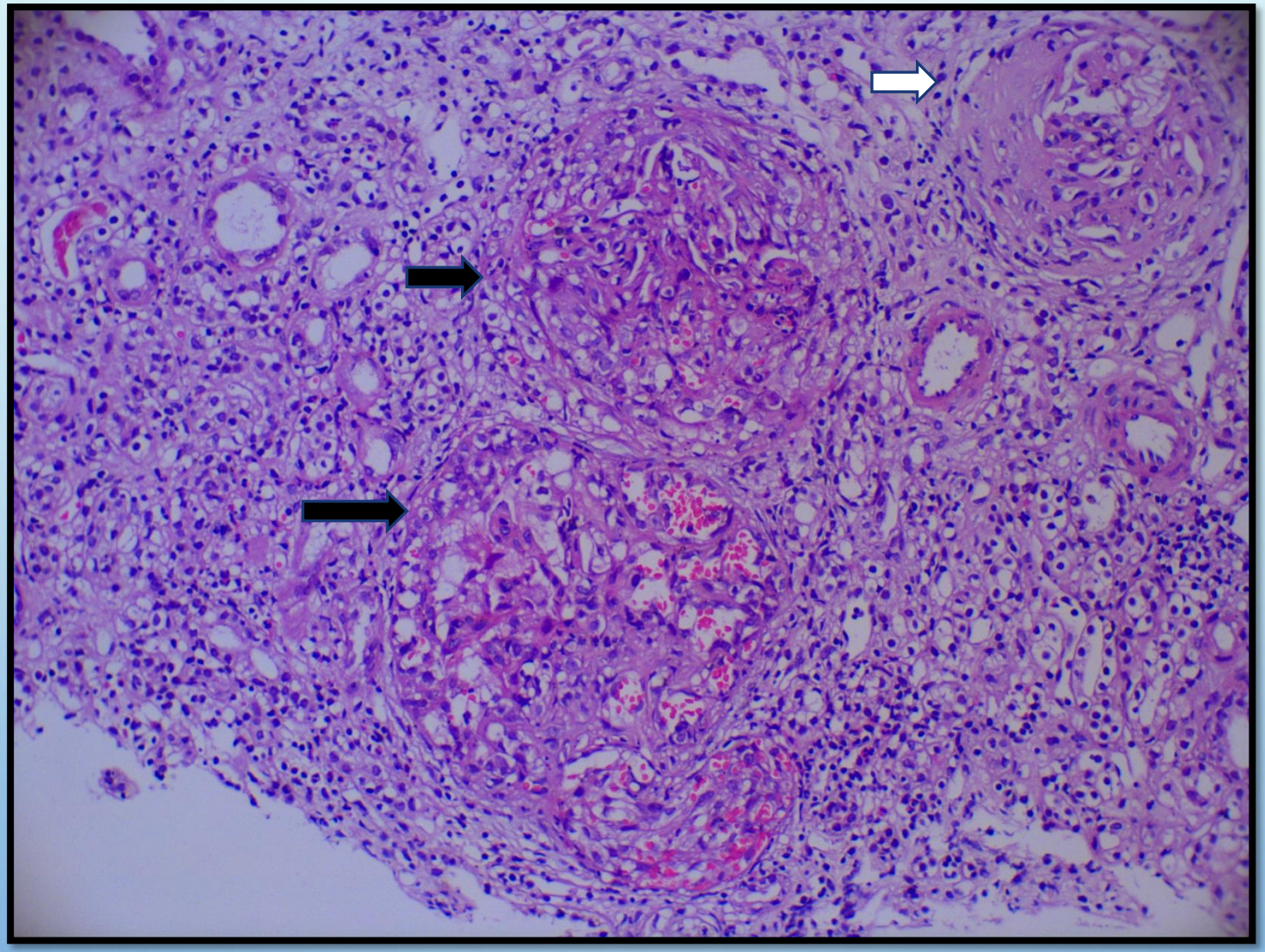
# PROVISIONAL DIAGNOSIS

| AKI | Vs. | RPRF |
|---|---|---|
| Urosepsis | | ANCA GN<br><br>Anti GBM Ab Disease<br><br>IgA Nephropathy with crescents |

# LAB REPORTS PART 2

- C3/ C4- normal
- ANA Blot- negative
- cANCA/pANCA- negative
- **Anti GBM Ab- Positive (76.83 RU/ml)**
- HRCT chest done to r/o Pulmonary renal syndroem- no e/o alveolar haemorrhage
- Urine culture- E. coli(>1,00,000 cfu/ml)

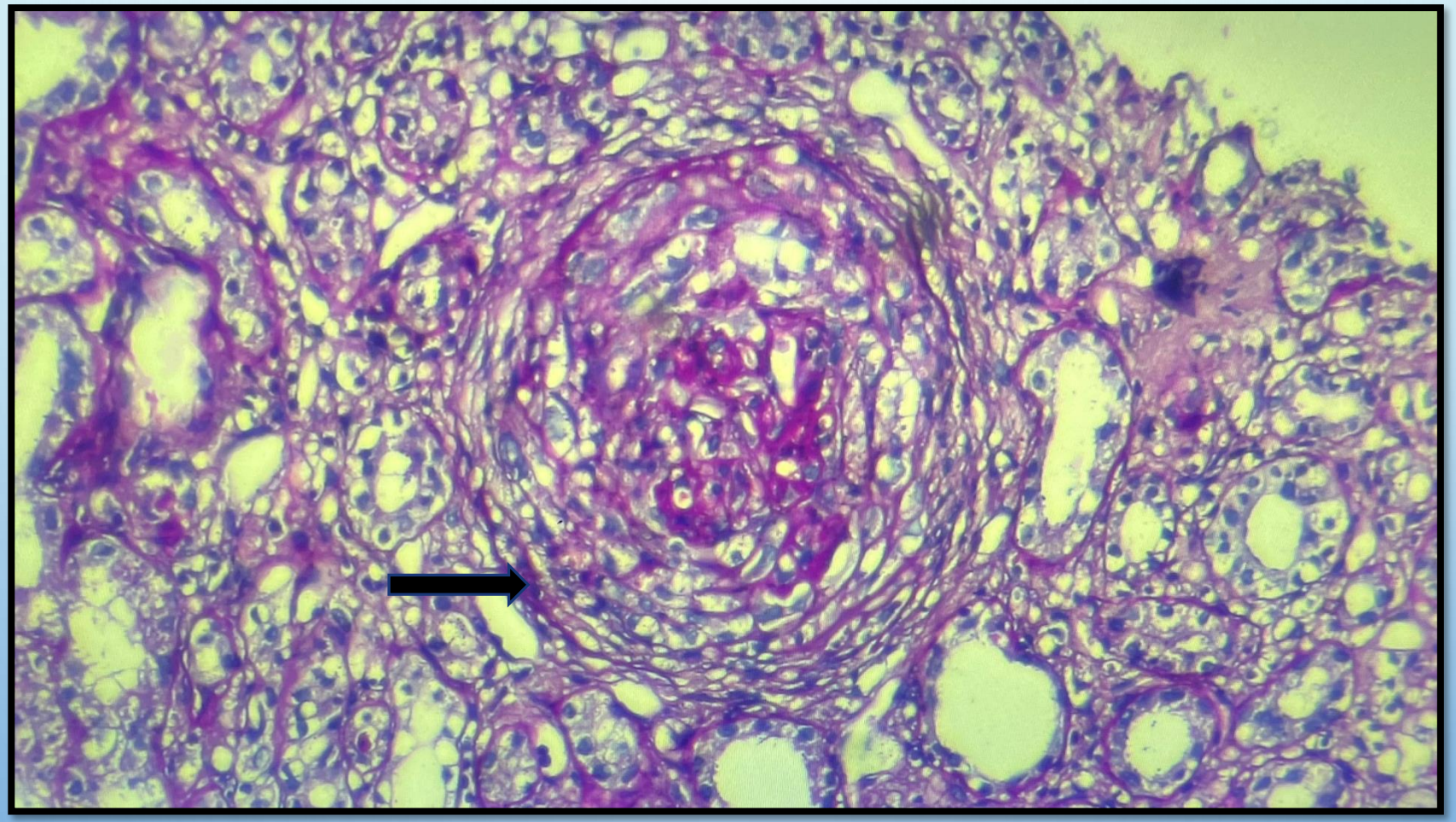
- Patient treated with culture specific antibiotics and underwent **RENAL BIOPSY**.



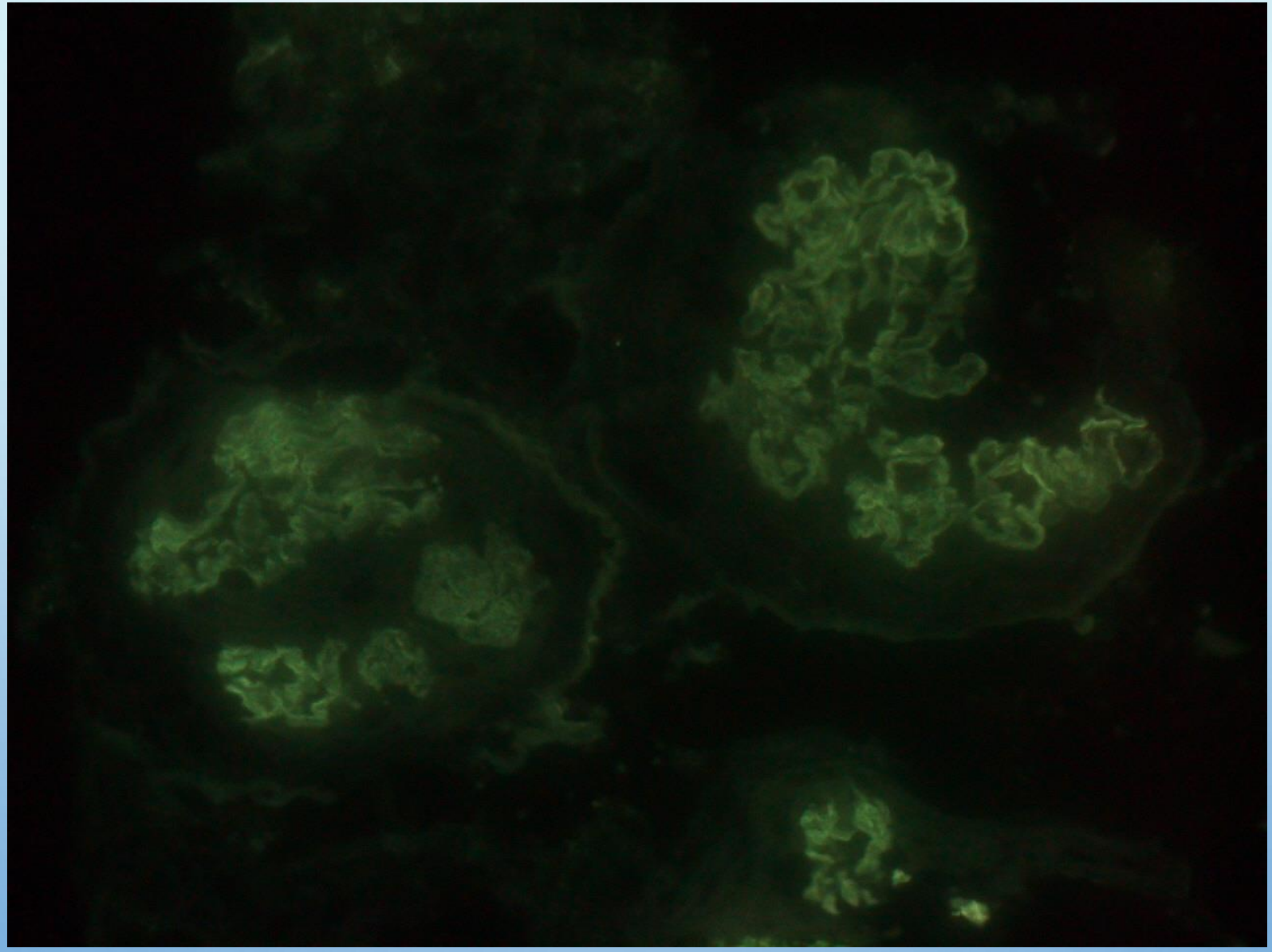
**Kidney histopathology slide, H& E stain, 3 glomeruli seen, black arrows showing cellular crescents, white arrow showing fibrous crescent**

# RENAL BIOPSY

- 9/19 glomeruli global sclerosis, crescents seen ( 10 cellular/4 fibrocellular/2 fibrous)
- Tubules showed RBC casts, tubular atrophy noted (50%)
- Interstitium- fibrosis(50%), lymphocyte and plasma cell infiltrate
- Immunofluorescence- linear IgG (+++) along the GBM



**Kidney histopathology slide, PAS stain, 1 glomerulus seen, black arrow showing cellular crescents**



**Kidney biopsy slide, immunofluorescence showing linear deposits of IgG along GBM**

- Electron microscopy report awaited.

# TREATMENT

- Patient initiated on haemodialysis through right IJV uncuffed HD catheter
- Inj. Methylprednisolone 250 mg i.v. OD given for 3 days f/b oral prednisolone 1mg/ kg/ day
- Plasmapheresis- single volume exchange, 35 ml/kg

# OUTCOME

- Till date, 5 cycles of PLEX done, alternate day with haemodialysis
- Urine output per day improved from 50 ml/ day to 600 ml/ day
- Hematuria subsided

# DISCUSSION

- GBM disease accounts for about 10% to 20% of crescentic glomerulonephritis.[1]
- This disease is characterized by circulating antibodies to the GBM (anti-GBM) and deposition of IgG or rarely, IgA along the GBM. [1]

Glassock RJ, Adler SG, Ward HJ, et al: Primary glomerular diseases. In Brenner BM, Rector FCJ, editors: *The kidney*, ed 4, Philadelphia, 1991, W.B. Saunders Company, pp 1182–1279.

- Anti-GBM disease occurs as

1. Renal-limited disease (anti- GBM glomerulonephritis)

2. Pulmonary-renal vasculitic syndrome (Goodpasture's syndrome)

- **The first peak**

-2nd and 3rd decades of life

-higher frequency of pulmonary hemorrhage

(Goodpasture's syndrome).

- **The second peak**

-6th and 7th decades

-more common in women

-renal limited disease

# PATHOLOGY

- **Immunofluorescence Microscopy**
- The diagnostic finding linear staining of the GBMs for immunoglobulin predominantly IgG; rare cases of IgA dominant
- Linear staining for both κ- and λ-light chains typically accompanies the staining for γ-heavy chains.

# PATHOLOGY

- **Immunofluorescence Microscopy**
- The linear IgG staining of GBMs frequently seen in diabetic glomerulosclerosis and the less intense linear staining seen in older patients with hypertensive vascular disease
- The clinical data and light microscopic findings should help make this distinction.
- Serologic confirmation

# LIGHT MICROSCOPY

- 97% of patients have some degree of crescent formation.[2]
- 85% have crescents in 50% or more of glomeruli.[2]
- On average, 77% of glomeruli have crescents.[2]
- Glomeruli with crescents typically have fibrinoid necrosis in adjacent glomerular segments.
- Special stains like Jones' methenamine silver stain or periodic acid–Schiff stain, often demonstrate focal breaks in GBMs in areas of necrosis and also show focal breaks in Bowman's capsule.

Jennette JC: Rapidly progressive crescentic glomerulonephritis. *Kidney Int* 63:1164–1177, 2003.

# ELECTRON MICROSCOPY

- In acute disease- focal glomerular necrosis with disruption of capillary walls.
- Focal gaps in Bowman's capsule .
- **Fibrin tactoids**
- Cellular crescents with ultrastructural features of macrophages and epithelial cells.
- Absence of immune complex–type electron-dense deposits.

# PATHOGENESIS

- The landmark studies were those of Lerner, Glassock, and Dixon.[3]
- Antibodies eluted from kidneys of patients with Goodpasture's syndrome and injected into monkeys
- Glomerulonephritis, proteinuria, renal failure, and pulmonary hemorrhage along with intense staining of the GBM for human IgG.

Lerner RA, Glassock RJ, Dixon FJ: The role of anti-glomerular basement membrane antibody in the pathogenesis of human glomerulonephritis. *J Exp Med* 126:989–1004, 1967.

# PATHOGENESIS

- The antigen - collagenase-resistant part of type IV collagen, the noncollagenous domain (NC1 domain)
- About 90% of anti–type IV collagen antibodies are directed against the α3-chain of type IV collagen

# LABORATORY FINDINGS

- Acute nephritic syndrome with hematuria
- Dysmorphic erythrocytes and red blood cell casts
- Nephrotic-range proteinuria /nephrotic syndrome - rare
- The diagnostic laboratory finding - circulating antibodies to GBM, specifically to the α3-chain of type IV collagen.

- Detected in approximately 95% of patients

# DIAGNOSIS

- Serologic testing - anti-GBM Ab in suspects

-The immunoassays for anti-GBM antibodies may be negative in up to 10% of patients.[4]

- HRCT chest - to rule out pulmonary-renal syndrome
- Renal biopsy

**Tomino Y, Sakai H, Endoh M, et al: Detection of immune complexes in polymorphonuclear leukocytes by double immunofluorescence in patients with IgA nephropathy. *Clin Immunol Immunopathol* 24:63–71, 1982.**

# TREATMENT

- The standard treatment for anti-GBM disease is intensive plasmapheresis combined with corticosteroids and cyclophosphamide.[5,6]
- Plasmapheresis - replacement with a 5% albumin solution, daily basis until circulating antibody levels become undetectable.
- Patients with pulmonary hemorrhage- FFP at the end of each treatment.

5. Lockwood CM, Rees AJ, Pearson TA, et al: Immunosuppression and plasma-exchange in the treatment of Goodpasture's syndrome. *Lancet* 1:711–715, 1976.
6. KDIGO clinical practice guidelines on glomerular disease, June 2020

# TREATMENT

- Prednisolone - 1 mg/kg of body weight for at least the first month and then tapered over 3 months
- Cyclophosphamide- 2 mg/kg/day orally for 8 to 12 weeks.

# TREATMENT

- The role of high-dose intravenous methylprednisolone pulses remains unproven in the treatment of anti-GBM disease. [7]
- The urgent nature of the clinical process prompts to administer methylprednisolone (7 mg/kg daily for 3 consecutive days) as part of induction therapy in this and other forms of crescentic glomerulonephritis.

Glassock RJ: The role of high-dose steroids in nephritic syndromes: the case for a conservative approach. In Narins R, editor: *Controversies in nephrology and hypertension*, New York, 1984, Churchill Livingstone, p 421.

# TREATMENT

- Plasmapheresis + corticosteroids &cyclophosphamide - survival approx. 85%.
- Out of these , 40% progress to ESKD.[8]
- The major prognostic marker for the progression to ESKD – serum creatinine level at the time of initiation of treatment.
- Patients with a serum creatinine concentration higher than 5.6 mg/dL are unlikely to recover sufficient kidney function to discontinue renal replacement therapy.[9]

8. Peters DK, Rees AJ, Lockwood CM, et al: Treatment and prognosis in antibasement membrane antibody-mediated nephritis. *Transplant Proc* 14:513–521, 1982.

9.Savage CO, Pusey CD, Bowman C, et al: Antiglomerular basement membrane antibody mediated disease in the British Isles 1980-4. *Br Med J (Clin Res Ed)* 292:301–304, 1986.

# RECURRENCE

- Once in remission, recurrence is rare.[10]
- The recurrence after kidney transplantation -rare, after the disappearance or substantial diminution of anti-GBM antibodies.[10]

Rutgers A, Slot M, van PP, et al: Coexistence of anti-glomerular basement membrane antibodies and myeloperoxidase-ANCAs in crescentic glomerulonephritis. *Am J Kidney Dis* 46:253–262, 2005.

# FOLLOW UP

- Continue maintenance haemodialysis
- Monthly Anti GBM Ab titres
- Plan for renal transplant once titres undetectable for six months

# THANK YOU