athens-NEPHROLOGY

Rapidly Progressive Glomerulonephritis (RPGN)

Ταχέως εξελισσόμενη σπειραματονεφρίτιδα

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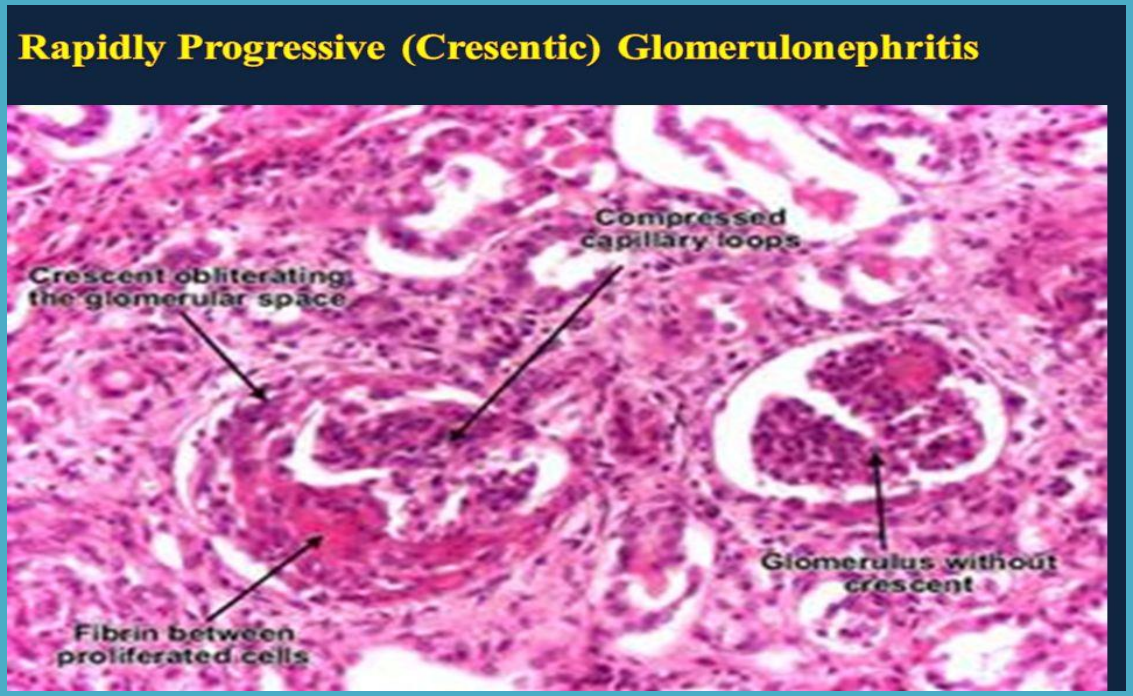
Νεφρολόγος



RPGN is NOT A SINGLE DISEASE ENTITY

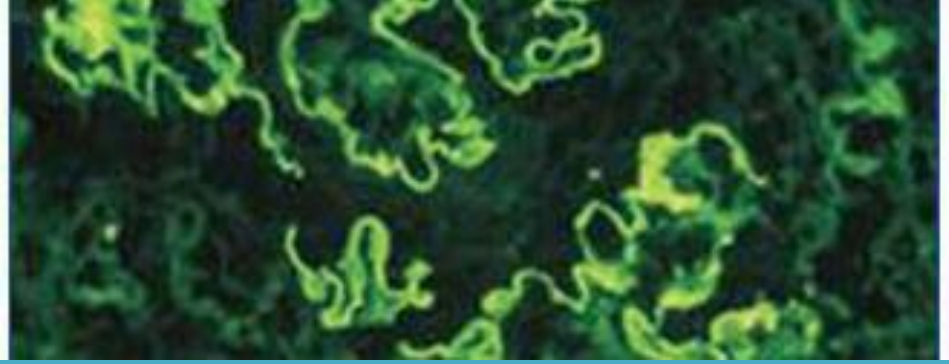
but

is a clinical syndrome that can result from a number of etiologies.

Rapidly progressive glomerulonephritis (RPGN).
RPGN consists of rapid loss of renal function with the histologic finding of crescent formation in more than 50% of glomeruli. These crescents represent a proliferation of cells within Bowman's space of the glomerulus due to the extravasation of proteins into this space. These cells comprise proliferating parietal epithelial cells as well as infiltrating macrophages and monocytes.

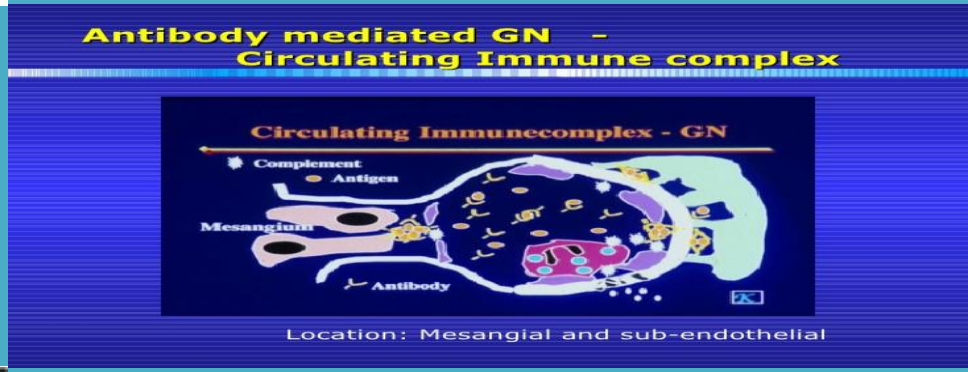
Rapidly Progressive Glomerulonephritis (RPGN)

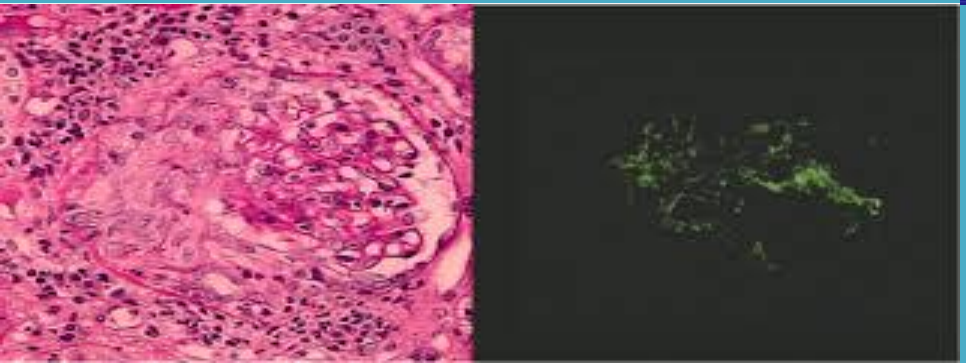
- Rapidly progressive renal failure
- Hematuria ± rbc casts; RBC dysmorphia
- Oliguria - variable
- Hypertension - unusual
- Proteinuria - variable



Linear deposits of IgG due to autoantibodies to Type IV collagen representing antiglomerular basement membrane (anti-GBM) glomerulonephritis (GN), which accounts for 15% of cases

Granular deposits of immune complexes caused by a variety of GNs including poststreptococcal GN, Henoch-Sch€onlein purpura, IgA nephropathy, membranoproliferativeGN, cryoglobulinemia, and lupus nephritis. Immunocomplex RPGN accounts for 24% of cases of RPGN.





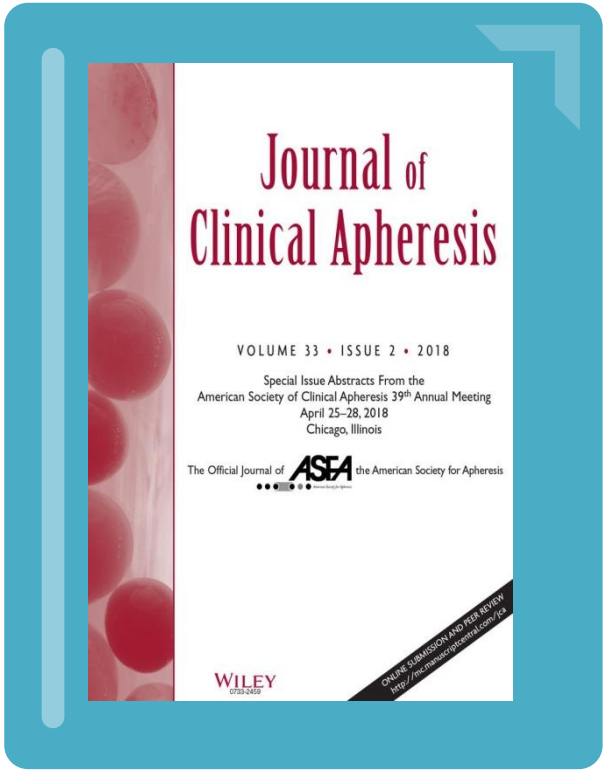
Minimal immune deposits in the glomerulus with the presence of antineutrophil antibodies [either CANCA (cytoplasmic) or P-ANCA (perinuclear)] in the serum.

Renal Biopsy

Necrotizing and/or Crescentic GN

Linear GBM deposits 11% (anti-GBM antibody disease)	Granular immune deposits 8% (immune complex disease)	No immune deposits 81% (ANCA-associated disease)
With pulmonary hemorrhage • Goodpasture syndrome Renal limited • Anti-GBM GN	Systemic symptoms • SLE • HSP • Postinfectious • Cryoglobulinemia Renal limited • IgA nephropathy • MPGN	Systemic symptoms •Wegener granulomatosis •Microscopic PAN •Churg-Strauss syndrome Renal limited •Pauci-immune GN

Percentages from Jennette, 1993; n = 65



Journal of Clinical Apheresis 31:149–162 (2016)

Guidelines on the Use of Therapeutic Apheresis in Clinical Practice—Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Seventh Special Issue

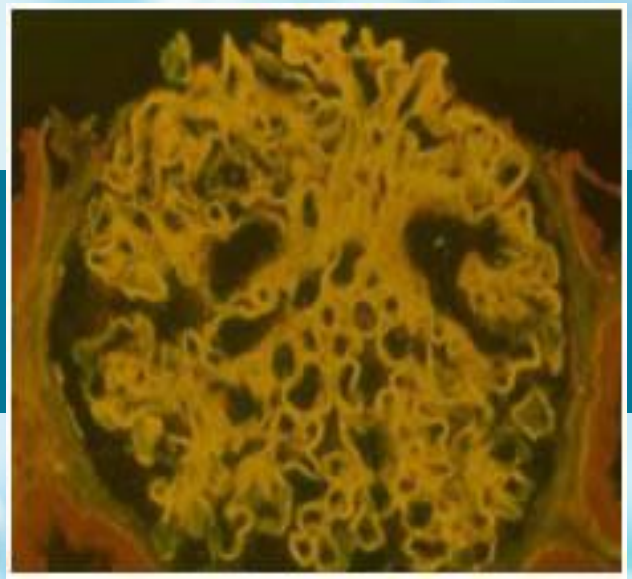
Joseph Schwartz,[1] Anand Padmanabhan,[2] Nicole Aqui,[3] Rasheed A. Balogun,[4] Laura Connelly-Smith,[5] Meghan Delaney,[6] Nancy M. Dunbar,[7] Volker Witt,[8] Yanyun Wu,[9] and Beth H. Shaz[1,10,11]*

TABLE II. Category Definitions for Therapeutic Apheresis

Category	Description
I	Disorders for which apheresis is accepted as first-line therapy, either as a primary standalone treatment or in conjunction with other modes of treatment.
II	Disorders for which apheresis is accepted as second-line therapy, either as a standalone treatment or in conjunction with other modes of treatment.
III	Optimum role of apheresis therapy is not established. Decision making should be individualized.
IV	Disorders in which published evidence demonstrates or suggests apheresis to be ineffective or harmful. IRB approval is desirable if apheresis treatment is undertaken in these circumstances.

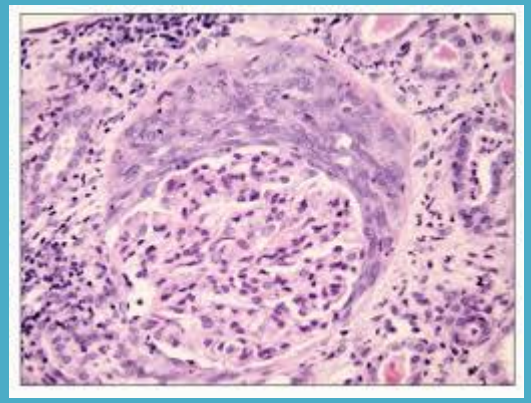
TABLE III. Grading Recommendations Adopted from Guyatt et al. [4,9]

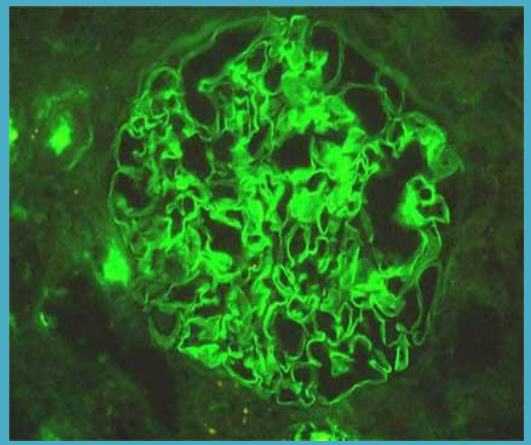
Recommendation	Description	Methodological quality of supporting evidence	Implications
Grade 1A	Strong recommendation, high-quality evidence	RCTs without important limitations or overwhelming evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
Grade 1B	Strong recommendation, moderate quality evidence	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
Grade 1C	Strong recommendation, low-quality or very low-quality evidence	Observational studies or case series	Strong recommendation but may change when higher quality evidence becomes available
Grade 2A	Weak recommendation, high-quality evidence	RCTs without important limitations or overwhelming evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
Grade 2B	Weak recommendation, moderate-quality evidence	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
Grade 2C	Weak recommendation, low-quality or very low-quality evidence	Observational studies or case series	Very weak recommendations; other alternatives may be equally reasonable



Description of the disease

Goodpasture's syndrome (GS) is a rare and organ-specific autoimmune disease. It is mediated by anti-glomerular basement membrane (anti-GBM) antibodies directed against a domain of α3 chain of Type IV collagen, causing activation of the complement cascade, resulting in tissue injury due to a classic Type II reaction. Only alveolar and GBM are affected, therefore, symptoms include crescentic or rapidly progressive glomerulonephritis (RPGN) and diffuse alveolar hemorrhage (DAH). Up to 30–40% of patients have been reported to have only renal limited involvement. Pulmonary symptoms range from breathlessness to overt hemoptysis. Chest radiography is a useful tool in demonstrating DAH but findings are nonspecific. Anti-GBM is associated with a specific HLA allele, DRB1*1501. Almost all patients have anti-GBM antibodies detectable in their blood. Also, 30% of patients will also have detectable ANCA. Patients exhibiting both antibodies behave more like anti-GBM than ANCA-associated RPGN in the short-term but more like ANCA-associated RPGN in the long-term. GS affects more Caucasians than African Americans with a bimodal age distribution, 20–30 years and 60–70 years. GS has important differential diagnosis including Wegener granulomatosis, systemic lupus erythematosus, microscopic polyangiitis, other systemic vasculitis, and connective tissue diseases. Without treatment GS is a life threatening disease. It is important to identify the specific RPGN category in their patient as TPE treatment protocols and responses differ. Prognosis of GS is strongly correlated to an early treatment. The three principles are to rapidly remove circulating antibody, to stop further production of antibodies, and to remove offending agents (hydrocarbon fumes, metallic dust, tobacco smoke, infections [influenza A], cocaine, etc).





ANTI-GLOMERULAR BASEMENT MEMBRANE DISEASE (GOODPASTURE'S SYNDROME)

Incidence: 1/1,000,000/yr	Indication	Procedure	Recommendation	Category
	Dialysis-dependence[a], no DAH	TPE	Grade 2B	III
	DAH	TPE	Grade 1C	I
	Dialysis-independence[a]	TPE	Grade 1B	I
No. of reported patients: > 300	RCT	CT	CS	CR
	1(17)	0	19(468)	21

[a]At presentation, defined as Cr > 6 mg/dL. DAH = diffuse alveolar hemorrhage.

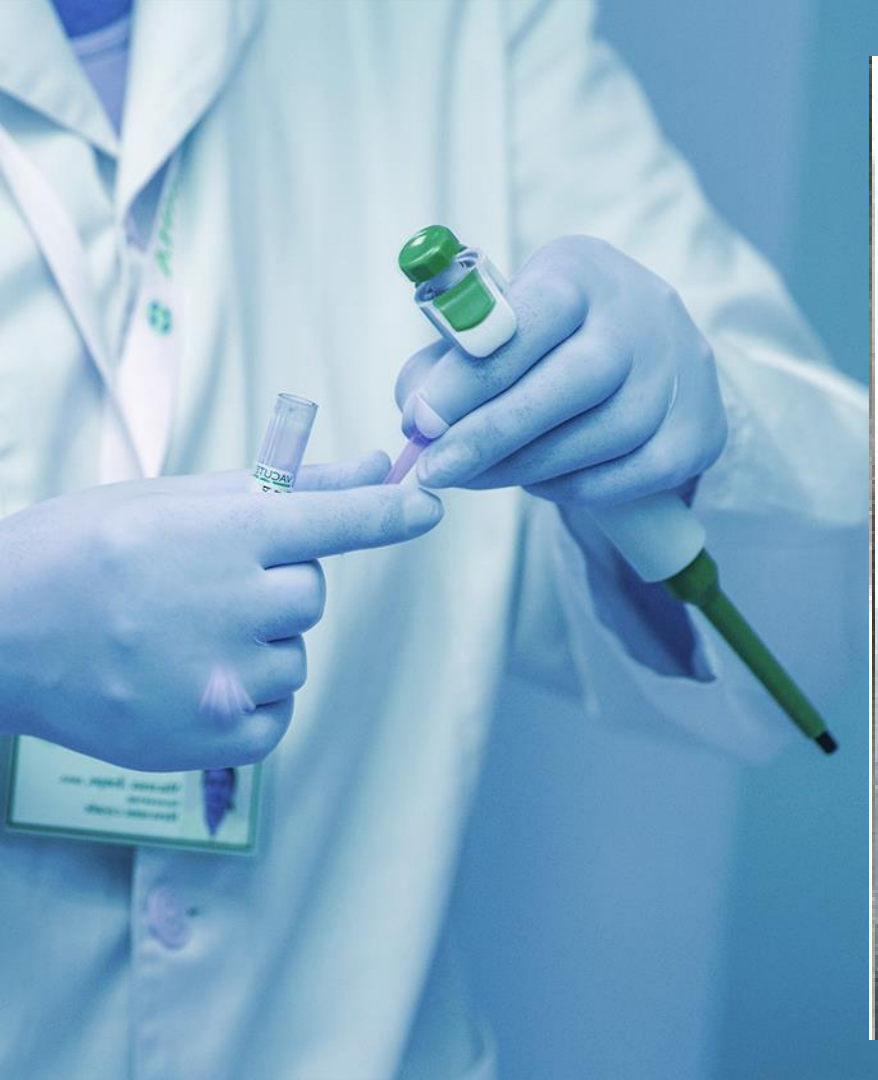
Technical notes

In the setting of DAH, plasma should be used for part or whole of the replacement fluid.

Volume treated: 1–1.5 TPV **Frequency**: Daily or every other day
Replacement fluid: Albumin; plasma when DAH present

Duration and discontinuation/number of procedures

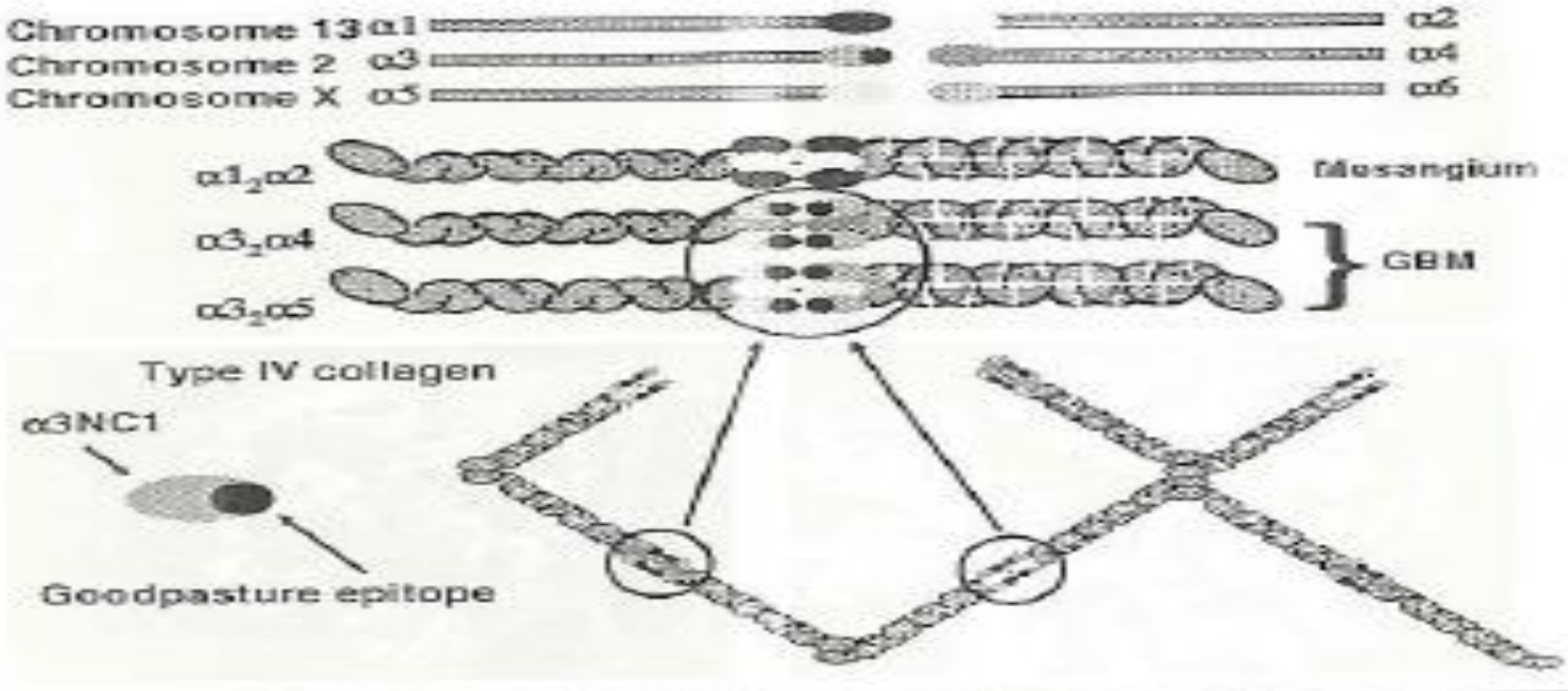
In most patients undergoing TPE and immunosuppression, anti-GBM antibodies fall to undetectable levels within 2 weeks; thus, the minimum course of TPE should be 10–20 days. The presence or absence of antibody should not be used to initiate or terminate therapy, because antibody is not demonstrable in a few patients with the disease and may be present in patients without active disease. In those patients with active disease, TPE should continue until resolution of evidence of ongoing glomerular or pulmonary injury.



What is the target antigen?

The NC1 domain of the α3 chain of type IV collagen

Location of the Goodpasture Antigen

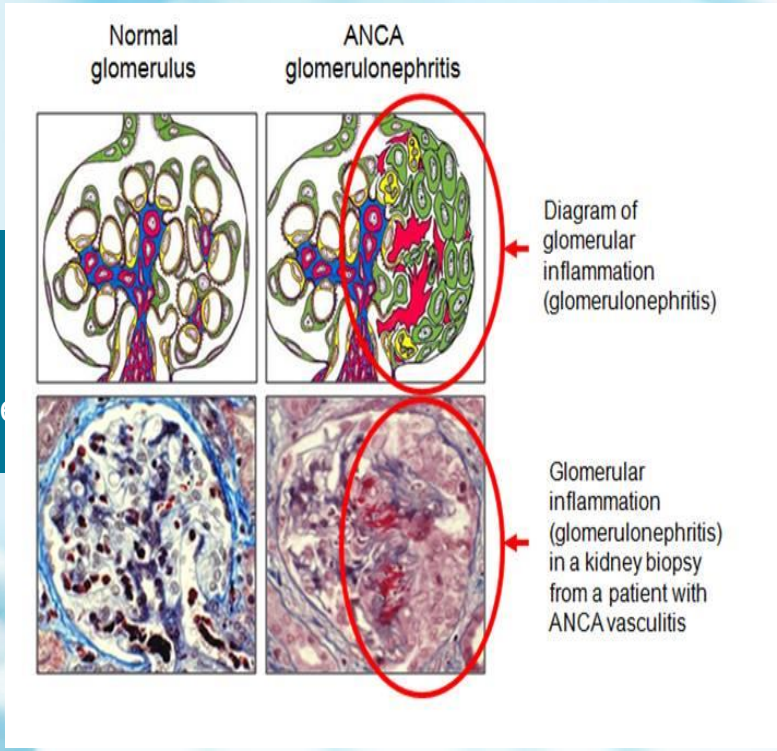


Anti-GBM Antibody Disease

Risk factors for pulmonary hemorrhage (Goodpasture syndrome):

- Young males
- Smoking, volatile solvents, viral respiratory infection

Ins


Normal glomerulus
ANCA glomerulonephritis
Diagram of glomerular inflammation (glomerulonephritis)
Glomerular inflammation (glomerulonephritis) in a kidney biopsy from a patient with ANCA vasculitis

Current management/treatment

Without treatment, GPA/MPA frequently progresses to ESRD over months. Symptoms include malaise, intermittent fever, weight loss, respiratory distress, and diffuse pain in joints and can culminate in mortality. The current management is combination therapy consisting of high-dose corticosteroids and cytotoxic immunosuppressive drugs (cyclophosphamide and rituximab). Two randomized trials indicate that rituximab is an effective alternative to cyclophosphamide in new or relapsing patients. Other drugs that have been used include leflunomide, deoxyspergualin, tumor necrosis factor blockers, calcineurin inhibitors, mycophenolate mofetil, and antibodies against T-cells. Overall, existing controlled trials suggest no benefit of TPE for many cases with kidney involvement. Important exceptions are: Patients with (1) severe active kidney disease, i.e., requiring dialysis therapy or with serum creatinine concentration above 6 mg/dL; (2) severe pulmonary hemorrhage; and (3) anti-GBM disease who are also ANCA-positive.

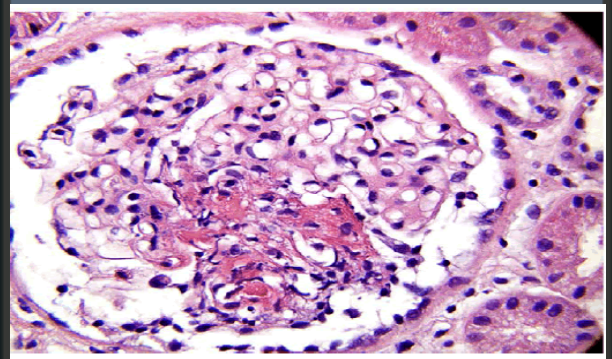


Figure 2: ANCA Vasculitis- Fibrinoid necrosis.

Incidence: 8.5/1,000,000/yr	**Indication**	**Procedure**	**Recommendation**	**Category**
	Dialysis dependence[a]	TPE	Grade 1A	I
	DAH	TPE	Grade 1C	I
	Dialysis independence[a]	TPE	Grade 2C	III
No. of reported patients: >300	**RCT**	**CT**	**CS**	**CR**
	8(296)	1(26)	22(347)	NA

[a]At presentation, defined as Cr >6 mg/dL. DAH = diffuse alveolar hemorrhage.

Rationale for therapeutic apheresis

The presence of ANCA autoantibodies indicates a humoral component in disease pathogenesis. TPE has been added in life-threatening cases, such as ANCA with DAH, and also in patients who are dialysis-dependent (or for whom initiation of dialysis is imminent). Much of the published experience with TPE includes all forms of RPGN, not exclusively GPA/MPA, which complicates data interpretation. Compared to the benefit of TPE in RPGN caused by anti-GBM, the benefit in type II (immune-complex) or III (GPA/MPA) RPGN is less certain. Six trials have examined the TPE in ANCA and immune-complex GNs. Of these, three prospective controlled trials consisting of a total 87 patients, found no benefit of TPE over standard therapy. Later subset analysis in two trials consisting of 62 patients found benefit in patients who were dialysis-dependent at presentation but not those with less severe acute kidney injury. Another trial consisting of 14 patients found benefit in all. Overall, these trials suggest that TPE is most beneficial in patients with dialysis-dependency (at presentation) and offers no benefit over immunosuppression in milder disease.

The role of TPE in GPA/MPA patients with advanced kidney impairment was addressed in MEPEX trial by the European Vasculitis Study Group. In this prospective study of 137 patients presenting with an initial diagnosis of ANCA-associated vasculitis with a serum creatinine >5.7 mg/dL, patients received standard therapy of oral corticosteroids and cyclophosphamide and were randomly assigned adjunctive therapy of either TPE or pulse methylprednisolone (1000 mg/day × 3 days). Mean baseline serum creatinine was 8.3 mg/dL and 69% required dialysis. Randomization to the treatment arm which included TPE (7 treatments over 14 days) was predictive of dialysis independence at 12 months (54% compared to 29%). TPE was also a positive predictor of recovery for those already on dialysis. High mortality (roughly 25%) occurred in both groups at one year. MEPEX was the largest study in a subsequent meta-analysis of 387 patients from nine trials, with creatinine levels ranging from 3.2 to 13.5 mg/dL. The addition of TPE to standard immunosuppression was associated with reduced risk of ESRD or death. Some more recent long-term (more than 10 years) outcome studies show that the short-term improved outcome in the TPE group may not be sustained long-term. A multicenter international RCT is in progress to ascertain the efficacy of TPE plus immunosuppressive therapy and glucocorticoids at reducing death and ESRD in ANCA positive vasculitis (PEXIVAS). RCTs of TPE in patients with RPGN and DAH have not been conducted. However, retrospective case series reported effective management of DAH in GPA/MPA.

Technical notes

In patients with DAH, replacement with plasma is recommended to avoid dilutional coagulopathy.

Volume treated: 1–1.5 TPV **Frequency**: Daily or every other day
Replacement fluid: Albumin; plasma when DAH present

Duration and discontinuation/number of procedures

Consider daily procedures in fulminant cases or with DAH then every 2–3 days for total of 6–9 procedures.

Does a rise in ANCA titer predict a relapse of vasculitis or GN?

- Patients with WG who had a rise in ANCA titer experienced fewer relapses if they were treated expectantly - *Cohen Tervaert et al. Lancet 1990*
- Meta-analysis showed only 48% specificity and 52% sensitivity - *Cohen Tervaert et al. 1995.*
- Relapse occurs more frequently in the presence of a positive ANCA (80% vs 20%) but a rise in titer is a poor predictor of relapse - *Kyndt et al. Am J Med 1999*

  PPV: cANCA 28%; anti-PR3 12%; anti-MPO 43%

Prognostic indicators in ANCA-associated GN

- With an alkylating agent, remission occurs in about 75%. Relapse occurs in about 30% of patients who achieve a remission, and in about 17% of patients after renal transplantation.
- Lung disease is a strong predictor of relapse and pulmonary hemorrhage accounts for at least half of all deaths.
- The risk of developing ESRD is directly related to the entry serum creatinine.
- Diagnostic category, severity of initial symptoms (mean vasculitis activity score, number of organs involved), and ANCA pattern do not significantly differ between relapsers and nonrelapsers.
- Persistently positive anti-MPO and proteinuria are predictors of ESRD.

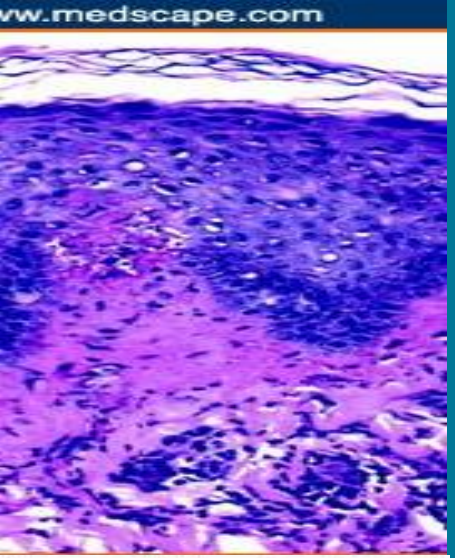
From: Nachman et al. Semin Nephrol 2000; Kyndt et al Am J Med 1999; Franssen et al JASN 1998.

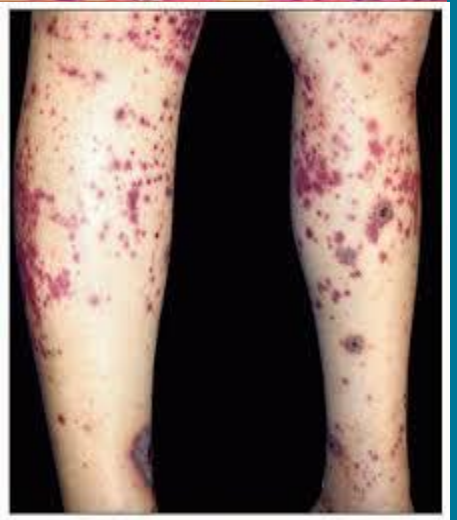
Drug-Associated ANCA-Positive Necrotizing Vasculitis

- Hydralazine
- Propylthiouracil
- Minocycline - HLA-DR4 or -DR2 linked
- Penicillamine
- Cimetidine
- Allopurinol
- Silicon ??

ANCA-associated GN - Summary

- ANCA is an excellent marker of crescentic GN without immune deposits.
- c-ANCA tends to occur more often in patients with features of classical Wegener's granulomatosis and p-ANCA in patients with renal limited disease but there is much overlap.
- MPO (p-ANCA)- and PR3 (c-ANCA)-associated GN and vasculitis have a similar prognosis and response to treatment.
- The titer of ANCA does not correlate well with disease activity but disappearance of ANCA is associated with remission.
- The value of ANCA in predicting relapse is controversial.
- Azathioprine is effective maintenance therapy.
- Plasmapheresis is indicated for AAGN vasculitis with ARF.





Immune complex disorders :

Postinfectious (staphylococci/streptococci)

Collagen-vascular disease

Lupus nephritis

Henoch-Schönlein purpura (immunoglobulin A and systemic vasculitis)

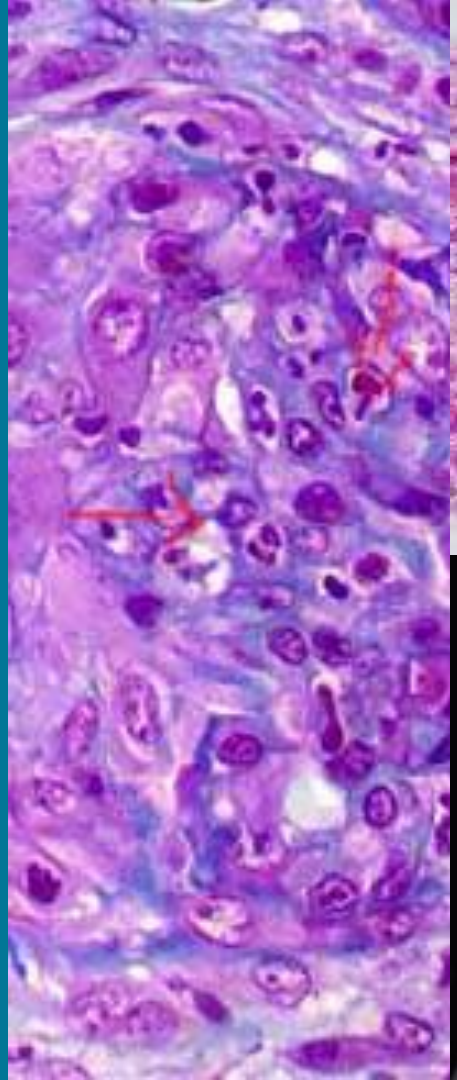
Immunoglobulin A nephropathy (no vasculitis)

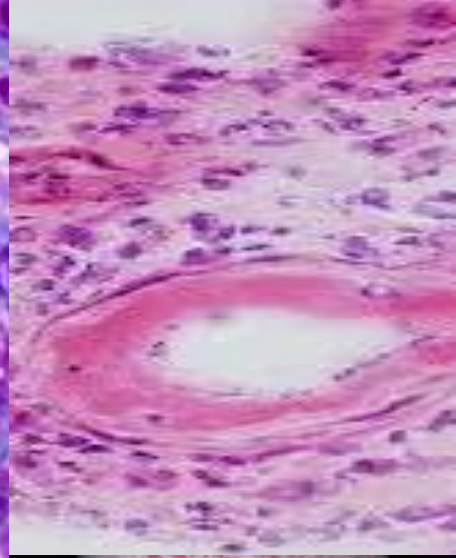
Mixed cryoglobulinemia

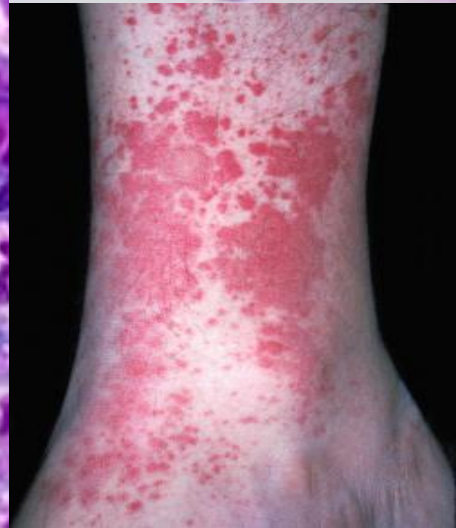
Membranoproliferative glomerulonephritis

Fibrillary glomerulonephritis

Idiopathic







HENOCH–SCHÖNLEIN PURPURA

Incidence: 13.5 to 22.1/100,000 with 1% developing RPGN	**Indication**	**Procedure**	**Recommendation**	**Category**
	Crescentic	TPE	Grade 2C	III
	Severe extrarenal manifestations	TPE	Grade 2C	III
No. of reported patients: < 100	**RCT**	**CT**	**CS**	**CR**
	0	0	8(65)	17(20)

RPGN = rapidly progressive glomerulonephritis.

Description of the disease

Henoch–Schönlein purpura (HSP) is the most common systemic vasculitis in childhood; 95% of HSP cases occur in children. HSP is almost always a self-limiting disorder, unlike most other forms of vasculitis. It presents with arthralgia/arthritis, abdominal pain, kidney disease, and palpable purpura in the absence of thrombocytopenia or coagulopathy. Characteristically, it occurs following an upper respiratory tract infection. The highest incidence of HSP is in Caucasians while African Americans have the lowest incidence. HSP is a systemic small vessel vasculitis characterized by deposition of IgA-containing immune complexes within tissues. All patients develop palpable purpura. In the skin, these deposits lead to subepidermal hemorrhages and small vessel necrotizing vasculitis producing the purpura. One-quarter to one-half of cases involve the kidney; IgA deposits within the mesangium of the glomerulus producing lesions ranging from mesangial proliferation to crescent formation and RPGN or crescentic glomerulonephritis, see Appendix and fact sheets on immune-complex rapidly progressive glomerulonephritis. IgG autoantibodies directed at mesangial antigens may also play a role in pathogenesis. Necrotizing vasculitis leads to organ dysfunction or hemorrhage in other organs.

In adults, the clinical presentation is more severe and outcomes are worse. Serum IgA levels were elevated in 60% of cases in one large adult series. Nonetheless, the precise role of IgA or antibodies to it in the pathogenesis of the disease remains unclear. In adults, the presence of interstitial fibrosis and glomerulosclerosis on kidney biopsy carries a poor prognosis. Reports of ESRD range from 15 to 30% over 15 years with additional cases advancing to Stage IV chronic kidney disease. A small percentage of patients will develop significant extrarenal dysfunction including cerebritis or severe GI bleeding.

Technical notes

Replacement fluid has varied depending upon the clinical situation with the final portion consisting of plasma in the presence of intracranial hemorrhage in cerebritis or GI bleeding. Double filtration plasmapheresis has also been used in a single patient with RPGN in HSP with resolution of renal disease.

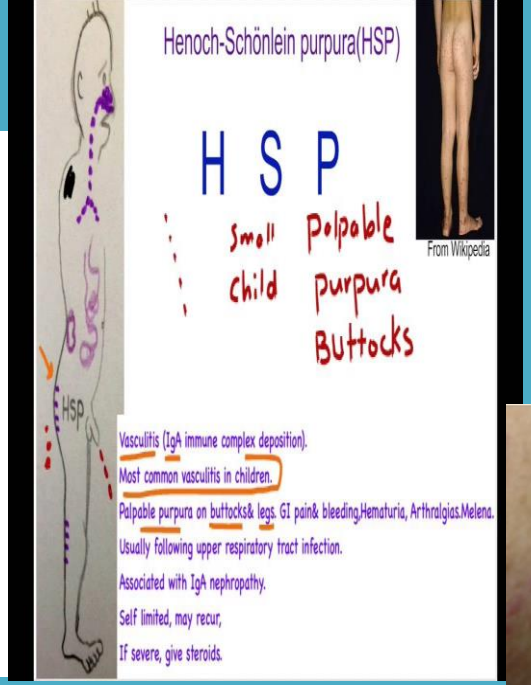
Volume treated: 1–1.5 TPV

Frequency: 4–11 over 21 days

Replacement fluid: Albumin

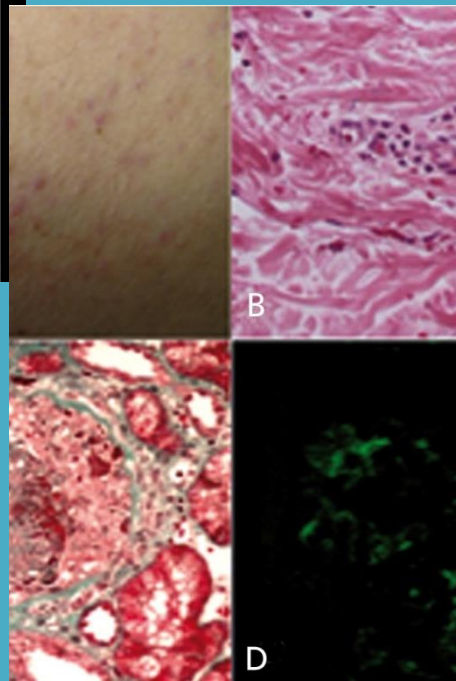
Duration and discontinuation/number of procedures

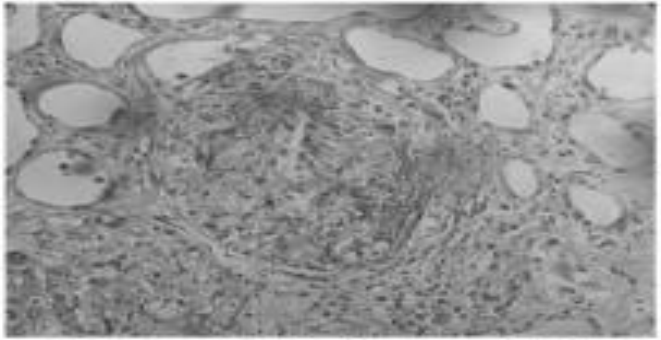
In cerebritis and severe GI manifestations, the course of therapy has ranged from one to six TPE daily with discontinuation of TPE upon resolution of symptoms. In RPGN, longer courses of therapy have occurred with therapy discontinued with improvement in renal function as determined by creatinine measurement.

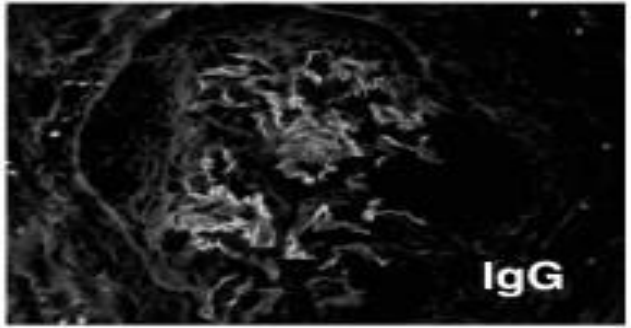


Current management/treatment

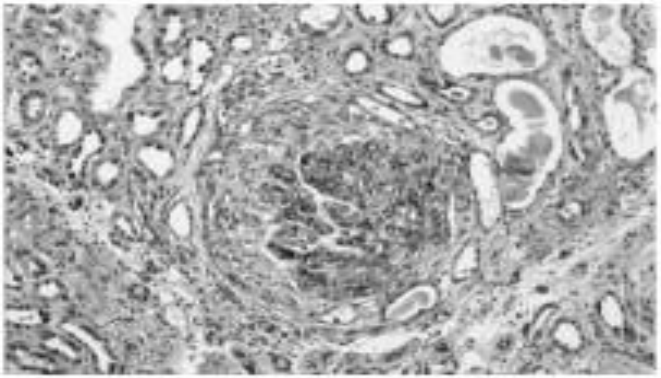
Treatment is supportive care including hydration, rest, and pain control. In patients with severe kidney involvement (i.e., RPGN or crescentic glomerulonephritis) or severe symptoms of vasculitis, treatment can also include corticosteroids with or without immunosuppressants such as cyclophosphamide, azathioprine, or cyclosporine and IVIG. If ESRD develops, kidney transplantation may be necessary.

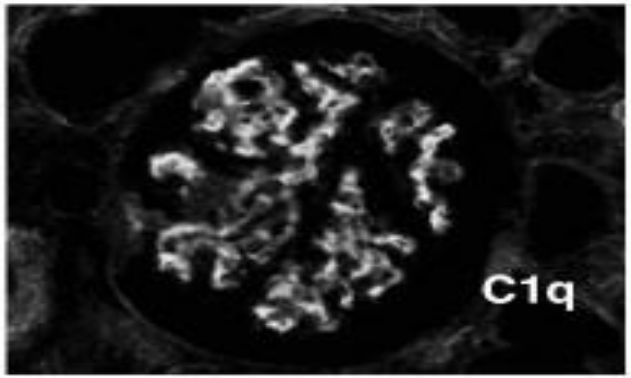




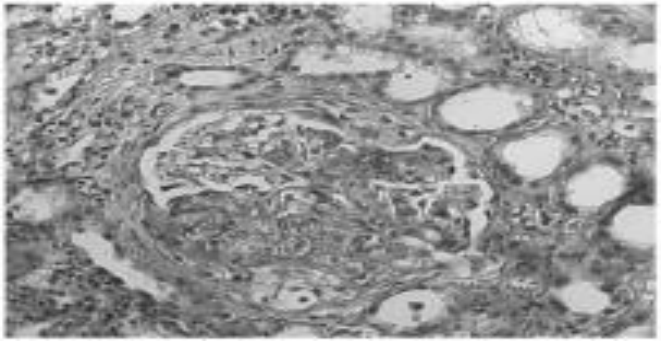


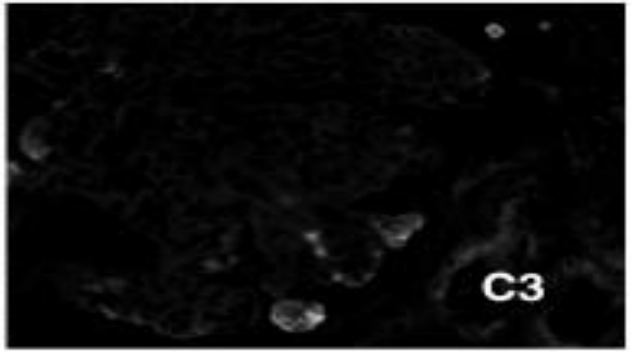
Goodpasture syndrome
Extracapillary proliferation and necrosis, no intracapillary proliferation. Linear deposits of IgG along the GBM





Lupus nephritis.
Extracapillary -and intracapillary proliferation. Granular deposits of C1q



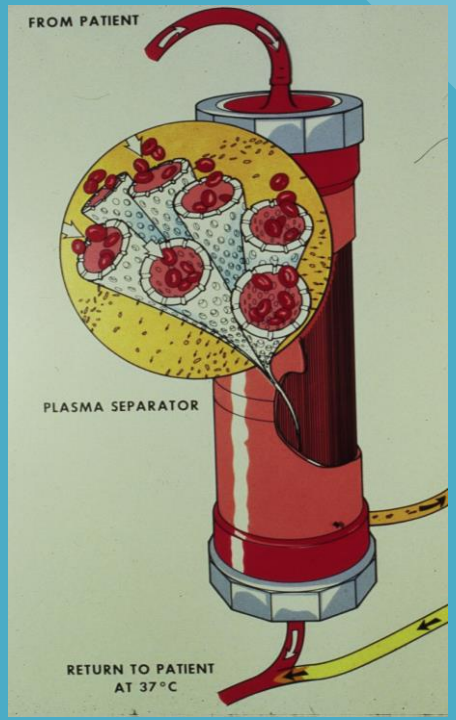


Granulomatosis with polyangiitis.
Extracapillary proliferation and necrosis. Faint deposits of C3

Current management/treatment

Therapy entails immunosuppressive agents: cyclophosphamide, azathioprine, prednisone, methotrexate, cyclosporine, and mycophenolate mofetil. Newer agents target abnormal immune cells, including rituximab, epratuzumab, and anti-dsDNA tolerogen LJP394. Other experimental approaches include inhibition of the CD40–CD40 ligand pathway, inhibition of the B7 pathway, IL-10 blockade of, and anti-tumor necrosis factor therapy. Belimumab, fully human monoclonal antibody (B-lymphocyte stimulator (BlyS) inhibitor), was recently approved for SLE treatment other than lupus nephritis or neuropsychiatric lupus (Boyce, 2012). Hematopoietic stem cell transplantation is a salvage therapy inducing long-term immunologic remission (Marmont, 2012): one study reported 76% 5 year survival.

SLEDAI (SLE Disease Activity Index) and SLAM (SLE Activity Measure) are used to determine disease activity and therapy effeciacy. SLEDAI consists of 19 items (present or absent) representing nine organ systems. SLEDAI score >5.0 defines active disease. SLAM includes 24 clinical manifestations for nine organ systems and eight laboratory variables, scored 0–2 or 0–3. Relationship between clinical impression and SLEDAI score has been recently evaluated: flare (increase in SLEDAI by >3), improvement (reduction of SLEDAI by >3), persistently active disease (change in SLEDAI $\pm \leq 3$), and remission (SLEDAI of 0).



SYSTEMIC LUPUS ERYTHEMATOSUS

Incidence: 15–50/100,000/yr	Indication	Procedure	Recommendation	Category
	Severe	TPE	Grade 2C	II
	Nephritis	TPE	Grade 1B	IV
No. of reported patients: > 300	**RCT**	**CT**	**CS**	**CR**
Severe	1(20)	1(4)	14(128)	> 50
Nephritis	4(78)	2(114)	6(160)	16(11)

Technical notes

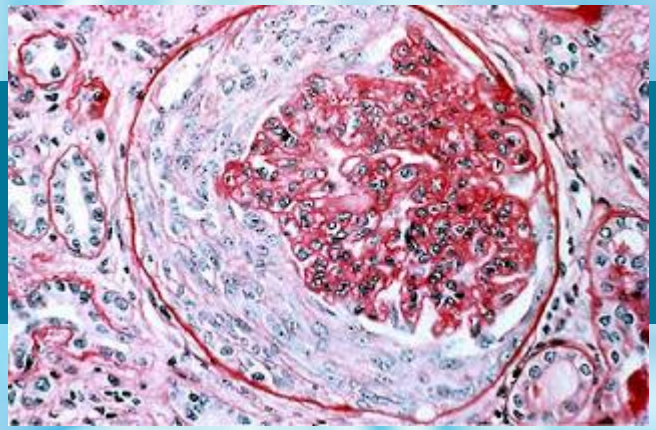
Volume treated: 1–1.5 TPV

Replacement fluid: Albumin, plasma

Frequency: Lupus cerebritis or DAH: daily or every other day; SLE other: 1–3 times per week

Duration and discontinuation/number of procedures

Typically course of 3–6 TPE is sufficient to see response in the patients with lupus cerebritis or DAH. Prolonged treatments have been reported but its efficacy and rationale is questionable.



Description of the disease

Immunoglobulin A nephropathy is the most common form of glomerulonephritis in the developed world, particularly in Asians and Caucasians. It is frequently asymptomatic with a benign course (no severe kidney damage) but there are reports of slow progression to end stage renal disease (ESRD) over 20 to 25 years in up to 50% of patients (chronic progressive) and, less commonly, the aggressive crescentic form can occur. Histologically, glomerular deposits of IgA characterize IgA nephropathy. Roughly >10% of patients can present as rapidly progressive crescentic glomerulonephritis (see immune-complex RPGN fact sheet). When there are symptoms, the classic presentation for the disease is gross hematuria occurring shortly after an upper respiratory infection (synpharyngitic) or, when asymptomatic, discovery of microscopic hematuria with or without proteinuria. Factors associated with disease progression are hypertension, persistent proteinuria >1,000 mg/day, and elevations in serum creatinine. The crescentic form is characterized by acute kidney injury with gross hematuria. While the pathophysiology has not been definitively characterized, current theory focuses on dysregulation of mucosal immune response: (1) mucosal B cells migrate to the bone marrow where they produce pathologic IgA1, (2) IgG antibodies are generated toward this IgA1, (3) IgA1-IgG and IgA1-IgA1 complexes are deposited in the mesangium of the glomerulus, (4) complement and mesangial IgA receptors are activated, (5) mesangial cell damage activates additional pathways, and (6) glomerulosclerosis and interstitial fibrosis develops. Evidence in support of this includes increased levels of serum IgA, the presence of poorly glycosylated IgA in the serum, and mesangial deposits of IgA. An increased level of plasma IgA alone, however, is insufficient to generate mesangial IgA deposits.

IMMUNOGLOBULIN A NEPHROPATHY

Incidence: 4/100,000 with 10% developing RPGN	Indication	Procedure	Recommendation	Category
	Crescentic	TPE	Grade 2B	III
	Chronic progressive	TPE	Grade 2C	III
# of reported patients: < 100	RCT	CT	CS	CR
	0	1(9)	7(64)	6(8)

RPGN = rapidly progressive glomerulonephritis.

Technical notes

Volume treated: 1–1.5 TPV

Replacement fluid: Albumin

Frequency: 6–9 over 21 days followed by 3–6 over 6 weeks.

Duration and discontinuation/number of procedures

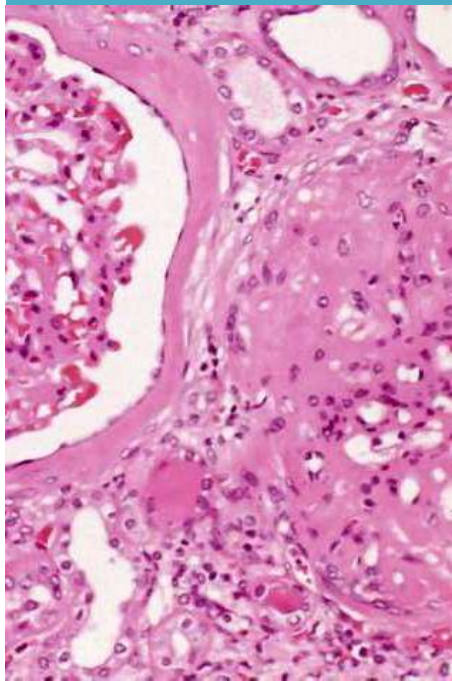
A fixed course of therapy has been used to treat patients presenting with RPGN. Creatinine is monitored to determine response. In chronic progressive disease, chronic therapy with weekly TPE for up to 4 months has been reported.

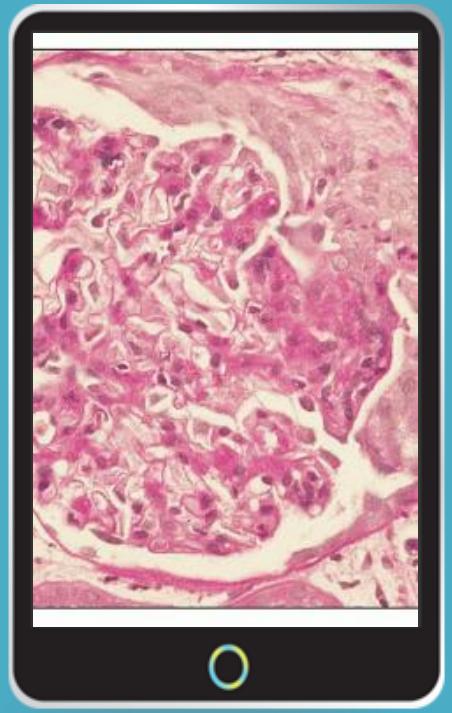
Rationale for therapeutic apheresis

The rationale for TPE in IGA nephropathy is for the removal of circulating pathologic IgA molecules and related immune complexes. Early positive experiences of the use of TPE in treating some forms of RPGN resulted in the application of TPE to cases presenting with RPGN (crescentic) form. In addition, early studies demonstrated that TPE could reduce the circulating IgA and IgA immune complexes levels. The majority of published experience has looked solely at the treatment of the RPGN form of the disease and not the chronic progressive disease.

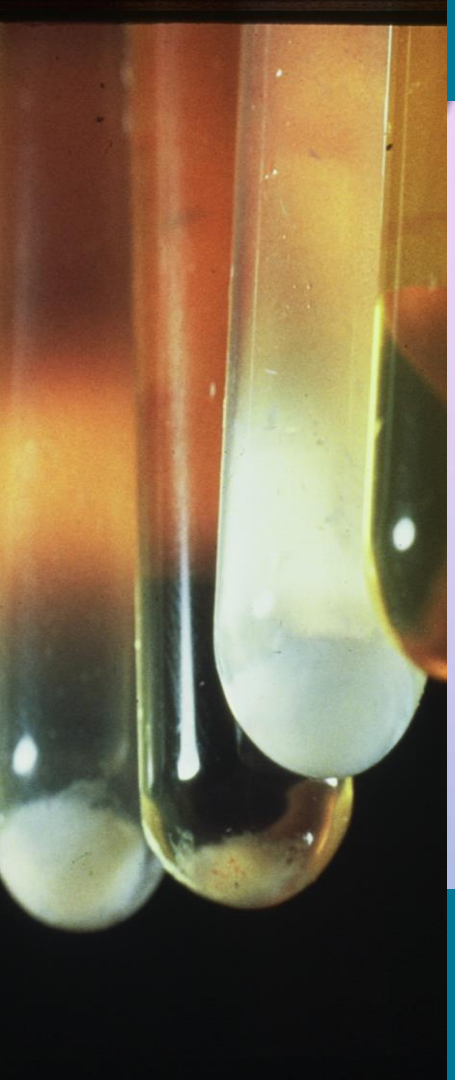
Case reports and case series from previous decades have addressed the treatment of the rapidly progressive form. The majority of these patients were treated with TPE and concurrent corticosteroids and/or immunosuppressants with reported improvement in kidney function and decrease in serum IgA. Numerous authors have found that improvement only occurred in the presence of cellular crescents, and not in sclerotic, scarred glomeruli. Two early reports involving 32 patients used only TPE, without other therapy, and saw improvement in kidney function in 31 of these patients. A controlled trial (Roccatello, 2000) examined three patients treated with corticosteroids and immunosuppressants and six who also received TPE. Two of the three patients who received only corticosteroids and immunosuppressants became dialysis dependent while the six receiving TPE demonstrated resolution of kidney failure during therapy. However, after discontinuation of TPE, disease progressed in all six, with three being dialysis dependent at 3 years following TPE and the remaining having mild to moderate chronic kidney disease. This trial is representative of the experiences reported in case series and case reports. TPE may improve function during therapy and delay the time to dialysis-dependence but does not halt disease progression.

Three case series have examined TPE in the chronic progressive form and have found improvement in renal function in 12 of 21 patients with slower disease progression during the course of TPE and a longer time to ESRD. All patients were receiving concurrent corticosteroids or immunosuppressant therapy. However, when TPE was discontinued, the rate of disease progression returned to that seen prior to initiation of TPE and all patients eventually progressed to ESRD.





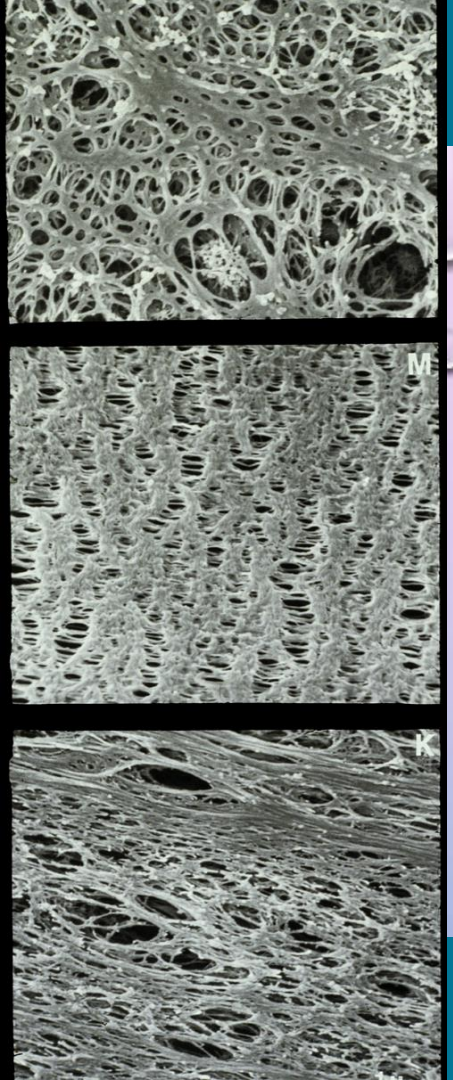
IgA Nephropathy and IgA Vasculitis (Henoch-Schönlein Purpura)



What is being removed?

Some **diseases** can create substances such as:

-**proteins, cytokines, toxins** or **antibodies** which circulate in the body through the **plasma portion** of the blood and can attack or damage healthy cells or tissues making the patient sick.



More specifically, it is removing autoantibodies in these autoimmune disorders such as:

Immune Thrombocytopenia (ITP), Autoimmune Hemolytic Anemia, Antiphospholipid crisis, Anti-GBM glomerulonephritis (& Goodpasture's), ANCA nephritis, ANCA vasculitis & Wegener's, Acute Guillain-Barré syndrome, Limbic Encephalitis, Chronic Inflammatory Demyelinating Polyneuropathy (CIDP), Myasthenia Gravis, Lambert-Eaton syndrome, Stiff Person syndrome, Acute Disseminated Encephalitis (ADEM), Neuromyelitis Optica (NMO), and some Multiple Sclerosis (MS).

On Average:

Plasmapheresis can take 90 – 140 min and patient should eat and be well hydrated prior to treatment.

Although, plasmapheresis is considered to be a safe procedure, it is not completely free of potential side effects.

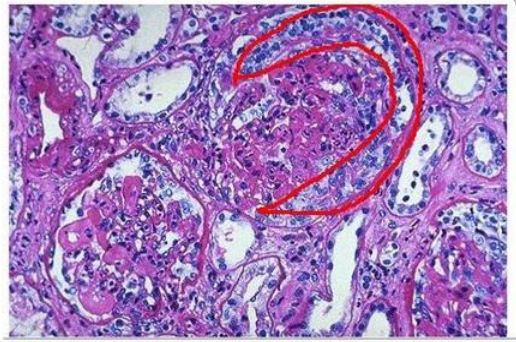
Side effects: citrate toxicity, hypocalcemia, hypotension, metabolic alkalosis, infection, or anaphylaxis.

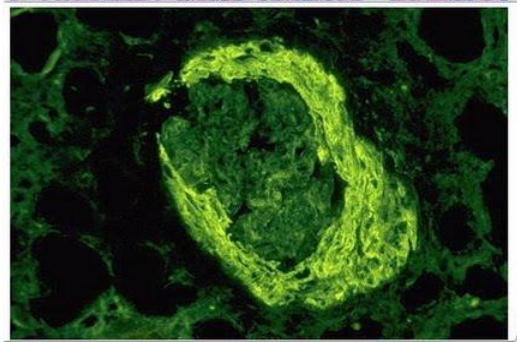
Rapidly Progressive GN

general characteristics
- clinical syndrome - not a specific etyologic form of GN
- those crescents are produced in part by proliferation of the parietal epithelial cells of Bowman's capsule in responce to injury and in part by infiltration of monocytes and macrophages
- pathogenesis
  - caused by a number of different diseases
    - kidney
    - systemic
  - most of the cases the injury is done by immunological pathways
  - classification of 3
    - **Anti-GBM 12%**
    - **Immune complex 44%**
    - **Pauci-immune (ANCA associated) 44%**

clinical features
- Rapid and progressive loss of renal function with features of nephritic Syndrome
- severe oliguria
- may require long-term dyalysis / transplantation
- **death from renal failure within weeks / months**
- those with crescents in less then 80% of glomeruli have better prognosis

characteristic histologic picture
- presence of crescents



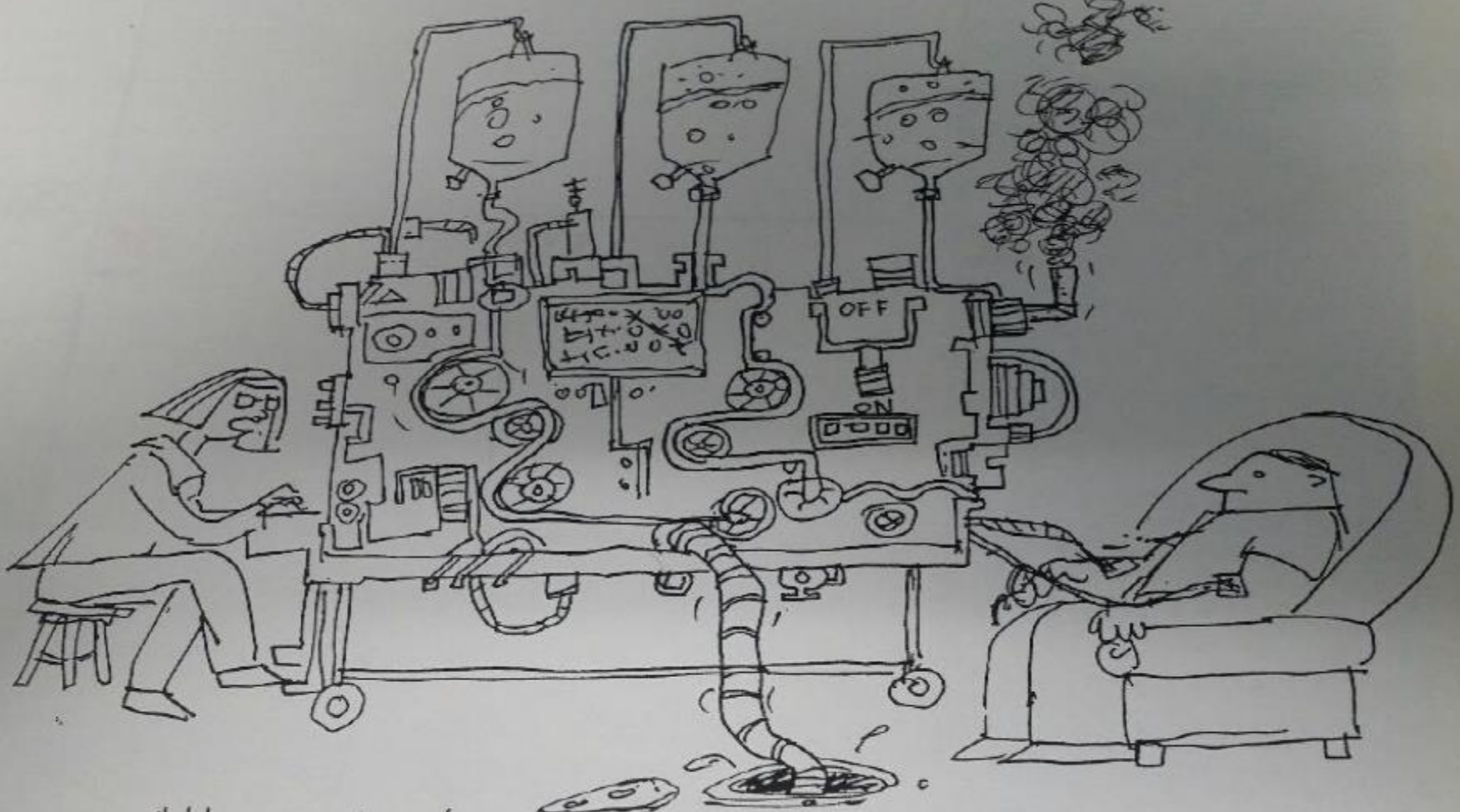


Anti-GBM
- characterised by
  - **linear depots of IgG and in many cases, C3 on the GBM**
  - **anti-GBM antibodies present in serum - helpful in diagnosis**
  - **benefit from plasmapheresis - removal of pathogen from blood**
- causes
  - Idiopathic
  - **Goodpasture**
    - renal impairment with pulmonary involvement
    - clinical picture of pulmonary hemorrhages with renal failure

Immune Complex
- characteristics
  - immune-complex disorders
  - **can be a complication of any of the immune complex nephritide**
    - SLE
    - post-streptococcal
    - IgA nephropathy
    - henoch-scholein purpura
  - granular pattern of staining of the GBM / mesangium
  - **cannot be helped with plasmapherisis**
- causes
  - Idiopathic
  - Henoch-Schonlein purpura
  - postinfectious
  - Hypersensitivity vasculitis
  - Cryoglobulinemia
  - SLE

Pauci-immune
- characteristics
  - defined by lack of anti - GBM antibodies or significant immune complex deposition
  - most of them have antineutrophil cytoplasmic antibodies
  - some cases are components of systemic vasculitis
  - pauci-immune is by definition, limited to the kidney
- causes
  - idiopathic
    - limited to kidney
  - Wegener's
  - Churg-Strauss
  - Microscopic Polyangitis
  - PAN

Crescents DO matter



"How about a tune, this thing is also a pianol"

QUESTIONS ????