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# Nephrologist, Pulmonologist Connection: From Bench to Bedside, Mini Review

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Mini Review

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Whether working in intensive care unit or not as nephrologists we are all facing complicated cases with different sign and symptoms. Among them is a category of patients presenting with concomitant respiratory and kidney failure called pulmonary renal syndrome, which needs mutual connection between nephrologist and pulmonologist closely for the best decision-making. Although this is not a common entity, still associated with high rate of morbidity and mortality involving diffuse alveolar hemorrhage and glomerulonephritis. Understanding the updates in the field of management would benefit both the patients and caregivers providing clear answers to present obstacles.

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## INTRODUCTION

Pulmonary renal syndrome including respiratory failure and acute kidney injury is not a solitary disease but is a wide spectrum of different entities mostly immune mediated systemic disorders, which cause inflammation in respiratory apparatus and proliferative glomerulonephritis simultaneously.[1] On the other hand Good-pasture disease specifically is known for crescentic glomerular involvement accompanied by alveolar hemorrhage associated with anti-glomerular basement membrane (anti-GBM) antibodies in circulation. Pulmonary renal syndromes predominantly are the consequences of systemic small vessel vasculitis and could be classified pathologically based on being Antineutrophil cytoplasmic antibody (ANCA) presence or absence for the ease of diagnosis. This family of vasculitis included primary systemic vasculitis especially granulomatosis with polyangiitis, microscopic polyangiitis, lupus and good-pasture syndrome.[2] One of the common concerns regarding this category is that these all can come up with an emergency condition without appropriate and on time medical care. Mainly the best result will earn when a multi-disciplinary team is involved in the management of patients. Pulmonary renal syndrome classification is summarized in Figure 1 based on predominant pathogenesis.

## GOOD-PASTURE DISEASE

Good-pasture or Anti-GBM disease is one of the pulmonary renal syndromes with immune-mediated pathogenesis affecting both kidney and

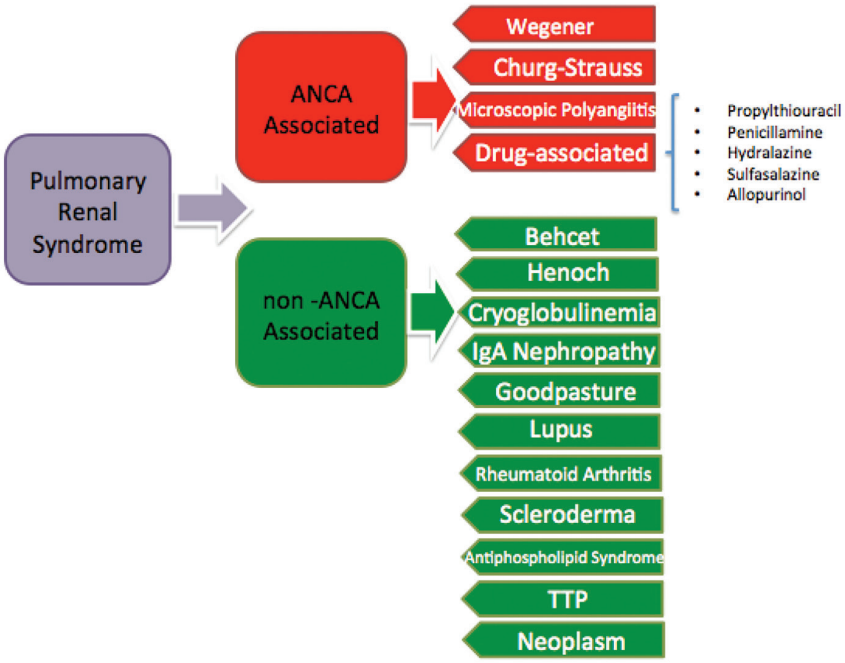


**Figure 1.** It determines pulmonary-renal Syndrome classification based on pathogenesis.

pulmonary system simultaneously. The target antigen, which is expressed both on alveolar capillaries and glomerular basement membranes, is the non-collagenous domain of alpha 3 chain of collagen type 4 and any simple event like a usual infection or any resembling peptides, which mimic this antigen, may expose this self-antigen to immune system.[3-5] Consequently a systemic inflammatory response would go on with no return point involving not only the humeral system but also cellular immunity with the presence of macrophages and T cells.[1,2] Post mortem autopsies from affected cases show massive alveolar hemorrhage accompanying by thickened alveolar walls with linear IgG deposition and edematous kidneys fully substituted with cellular or fibrous crescents and collapsed glomerular tufts again revealing linear IgG staining along GBM.

Early diagnosis and stepwise management is crucial and life saving as the Good-pasture holds a high rate of morbidity and mortality as well.

Currently standard of care for anti-GBM disease include therapies point toward removal of antibodies in first place plus inhibiting or at least reducing new antibody formation.[3] Deciding how to choose the best approach in these patients is a complicated decision, which should be made, based on taking both clinical and laboratory findings in to consideration .In Figure 2 a simplified algorithmic approach is shown for how to decide between different management plans in an individualized manner.

Another important and challenging issue in anti-GBM disease is how to sequentially monitor antibody titers in patient's follow-up visits in order to confirm relapsing episodes even though recurrent Good-pasture is a rare condition. Although anti-GBM antibodies reported to be self-limited in cases even without treatment but it is highly recommended to check the titers of antibody weekly during active phase of treatment with plasmapheresis and later every two weeks until two separate occasions come up with two negative results. How to periodically check the antibody titer is summarized in Figure 3. In case of the need for renal transplantation it is highly suggested that transplant procedure is better to postponed until the absence of anti-GBM antibody titers confirmed for an extended periods as recurrent disease after kidney transplantation is as high as 50% of cases.[5]

Treatment of choice in most of the anti-GBM disease cases is a combination of intensive plasmapheresis accompanying by aggressive immunosuppression therapy with corticosteroids and cyclophosphamide to remove circulating antibodies and meanwhile suppressing the new

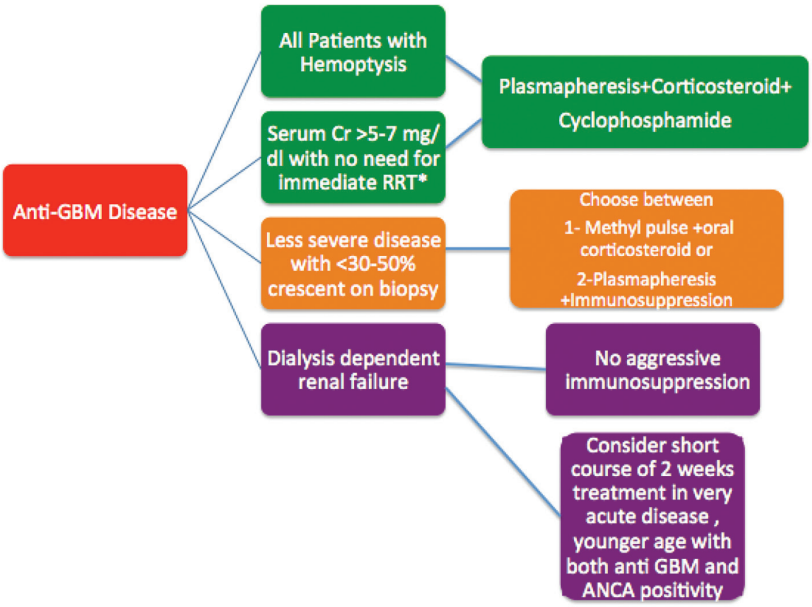


**Figure 2.** It mentions deciding how to manage anti-GBM disease based on clinical and para-clinical condition (*RRT: Renal Replacement Therapy).

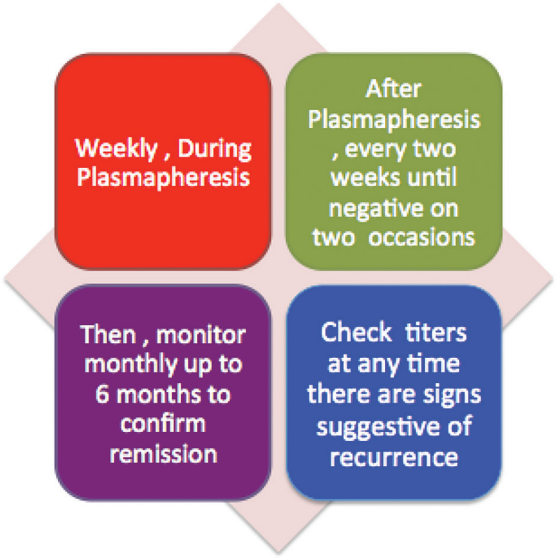


**Figure 3.** It shows how to sequentially monitor anti-GBM antibody titer.

antibody production as much as possible. Recovery would be much more achievable in patients who started treatment before oligoanuria has been established.[3]

In Table treatment of anti-GBM disease briefly is shown. Duration of treatment is mainly based on clinical remission and whenever negative titers of anti-GBM antibodies in serial detection occur. As a complication of plasmapheresis we should keep in mind the possibility of infections which make close follow up of patients in addition with wisely use of antibiotics mandatory.[4] Like many other life-threatening disease in medicine the corner stone of response to treatment and prognosis in long term is on time early diagnosis, which is not accessible unless a multidisciplinary team including concordant nephrologist-pulmonologist-intensivist be in charge of the patient care.

Treatment Options for Anti-GBM (Good-Pastures) Disease

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| Plasmapheresis | • Daily or Every Other Day<br>• 4 L Exchanges with Albumin<br>• In Hemodialysis or Risk of Bleeding Use 1-2 L FFP<br>• Continue 2-3 Weeks |
| Corticosteroids | • 3 Days Methyl Pulse (1g) then<br>• 1 mg/kg/d Pred up to 60-80 mg/d<br>• Tapered to 20 mg/d by 3 Weeks<br>• Continue to 6 Weeks<br>• Slowly Tapered Until 6 Months |
| Cyclophosphamide | • Oral 2 mg/kg/d, 2-3 Months |
| Azathioprine | • If Anti-GBM Titers Remain Positive After 4 Months of Therapy, Continue Pred Alone or Pred+AZT (1-2 mg/kg/d) Up to 6-9 Months |

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