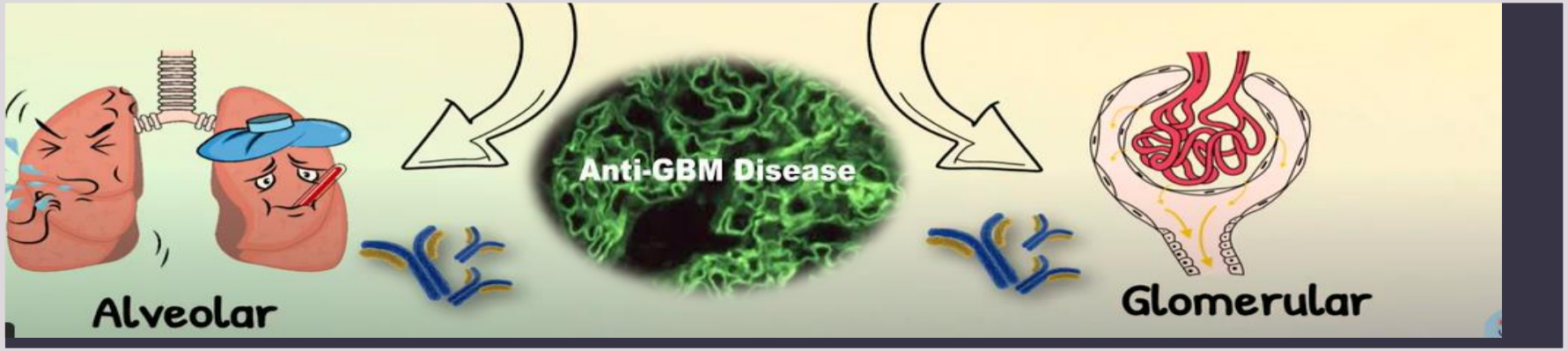

بسم الله الرحمن الرحيم

Anti-Glomerular Basement Membrane Disease(Anti-GBM Disease)



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Introduction

A type of small-vessel vasculitis-A rare glomerular disease

Autoantibodies targeting the noncollagenous domain of the α3 chain of type IV collagen(Kidneys and Lungs)

Bimodal Age distribution:3 th and 6 th decades of life

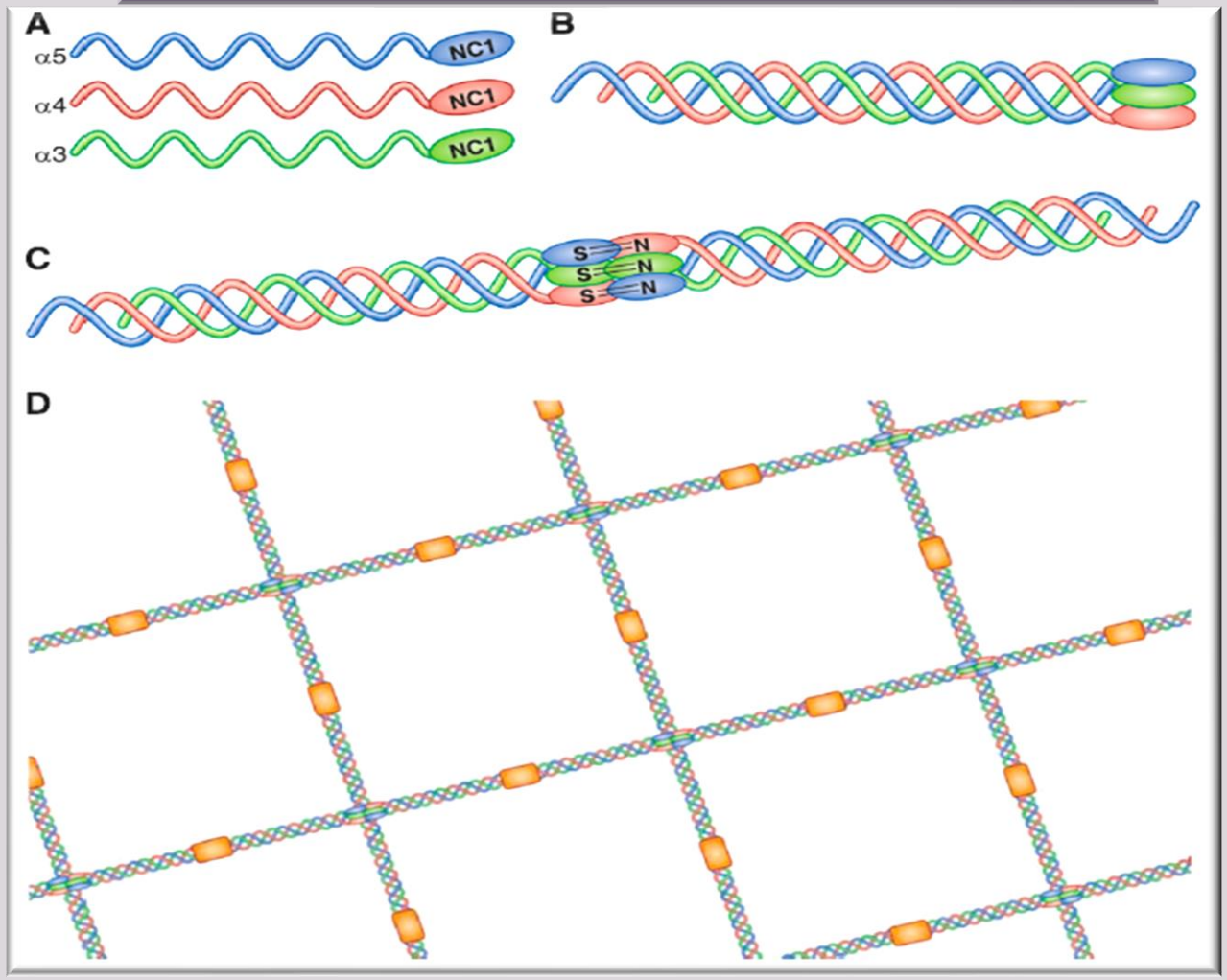
Introduction(con.)

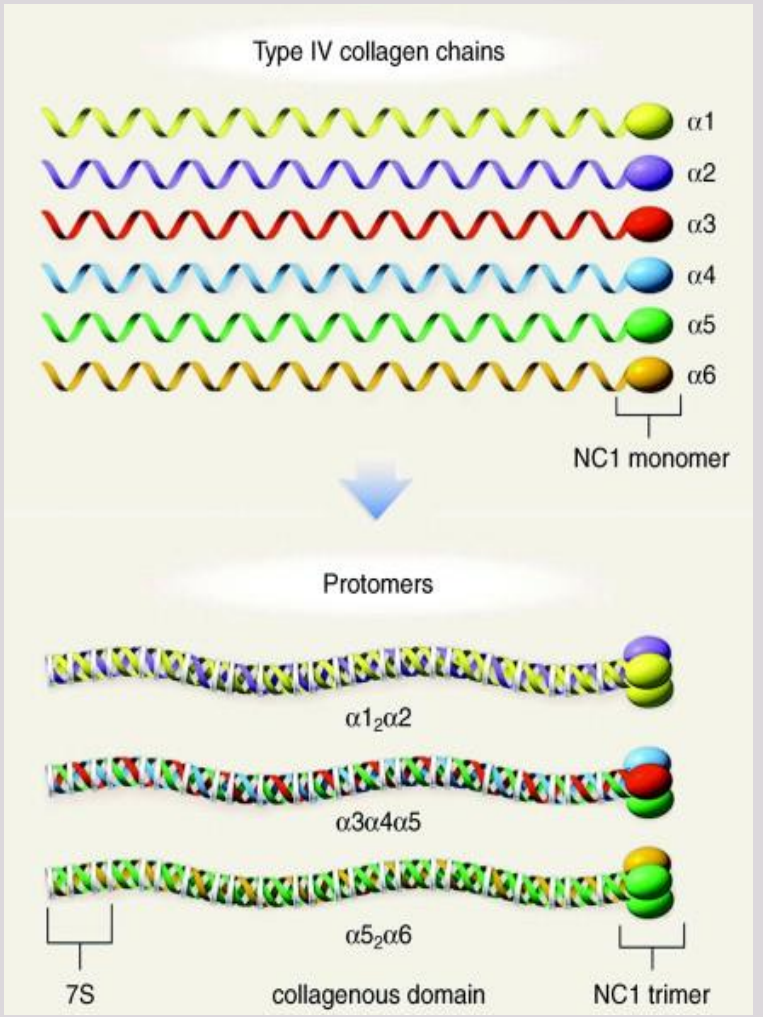
- Occur up to 30% concurrency with AAV
- Pulmonary-renal syndrome
- Isolated pulmonary hemorrhage is rare

https://doi.org/10.2215/CJN.01380217

Pathogenesis

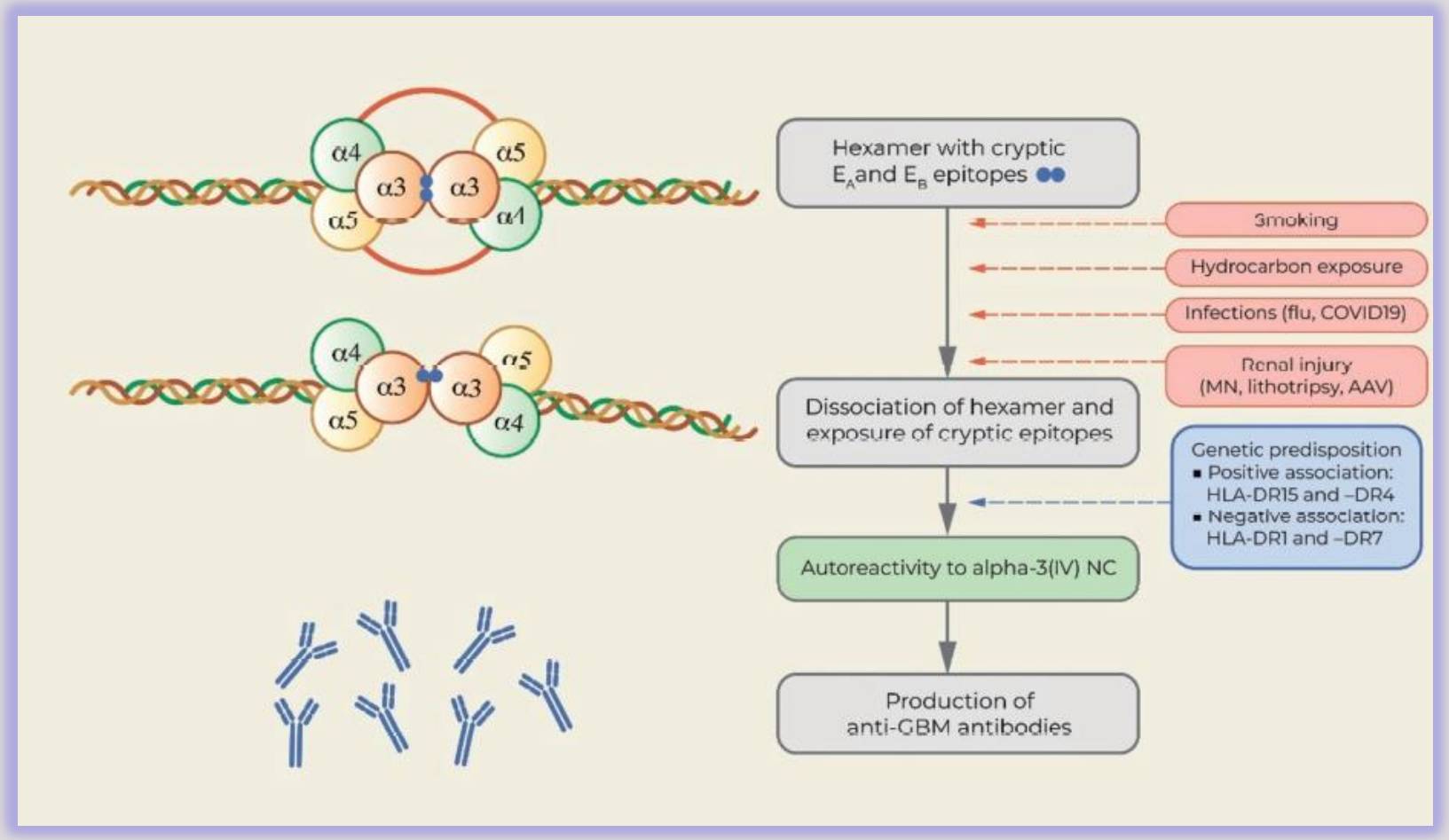
Structure of the glomerular basement membrane





Pathogenesis

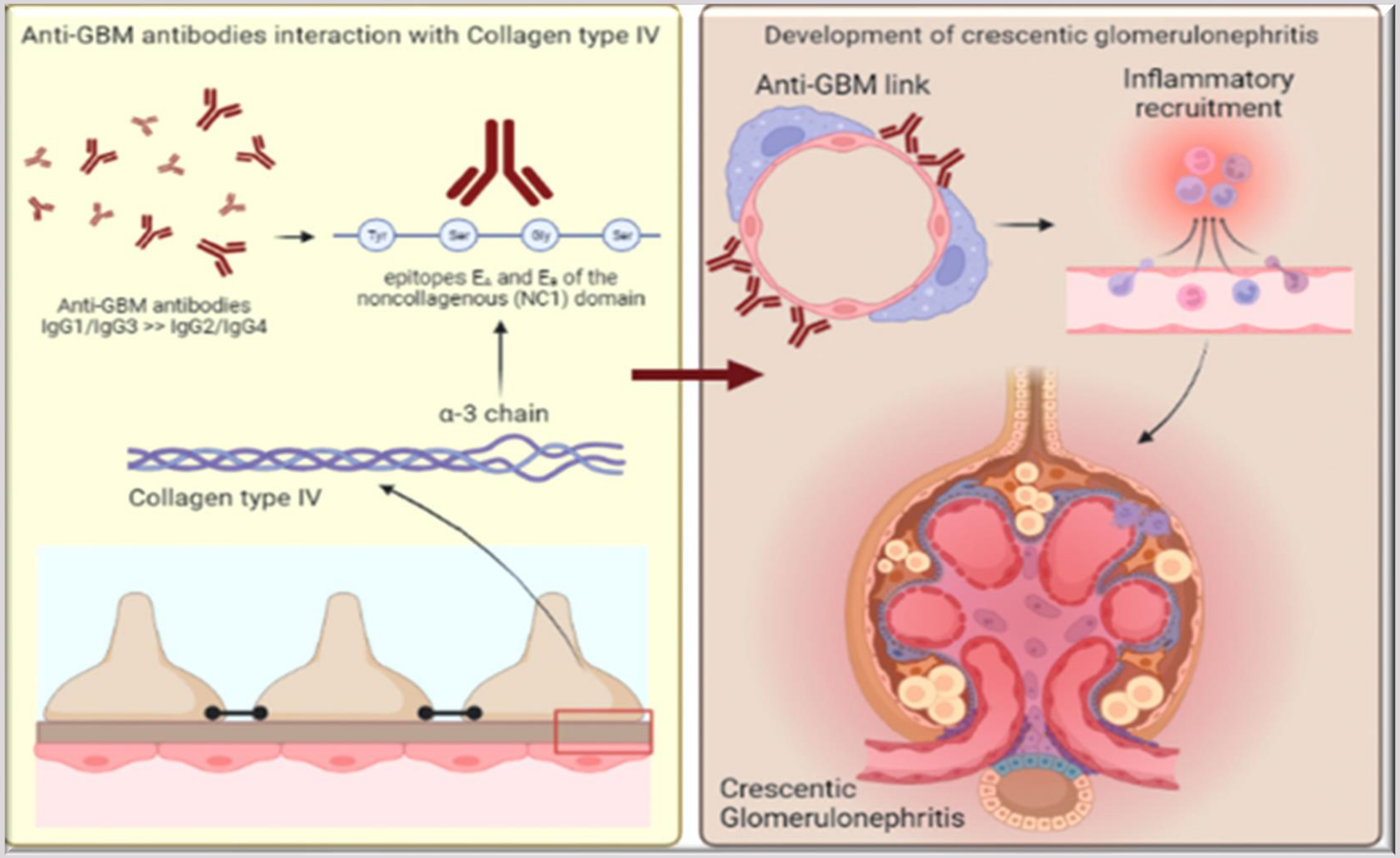
Schematic representation of anti-GBM Abs development



doi: 10.55563/clinexprheumatol/tep3k5

Pathogenesis

Schematic representation of anti-GBM glomerulonephritis



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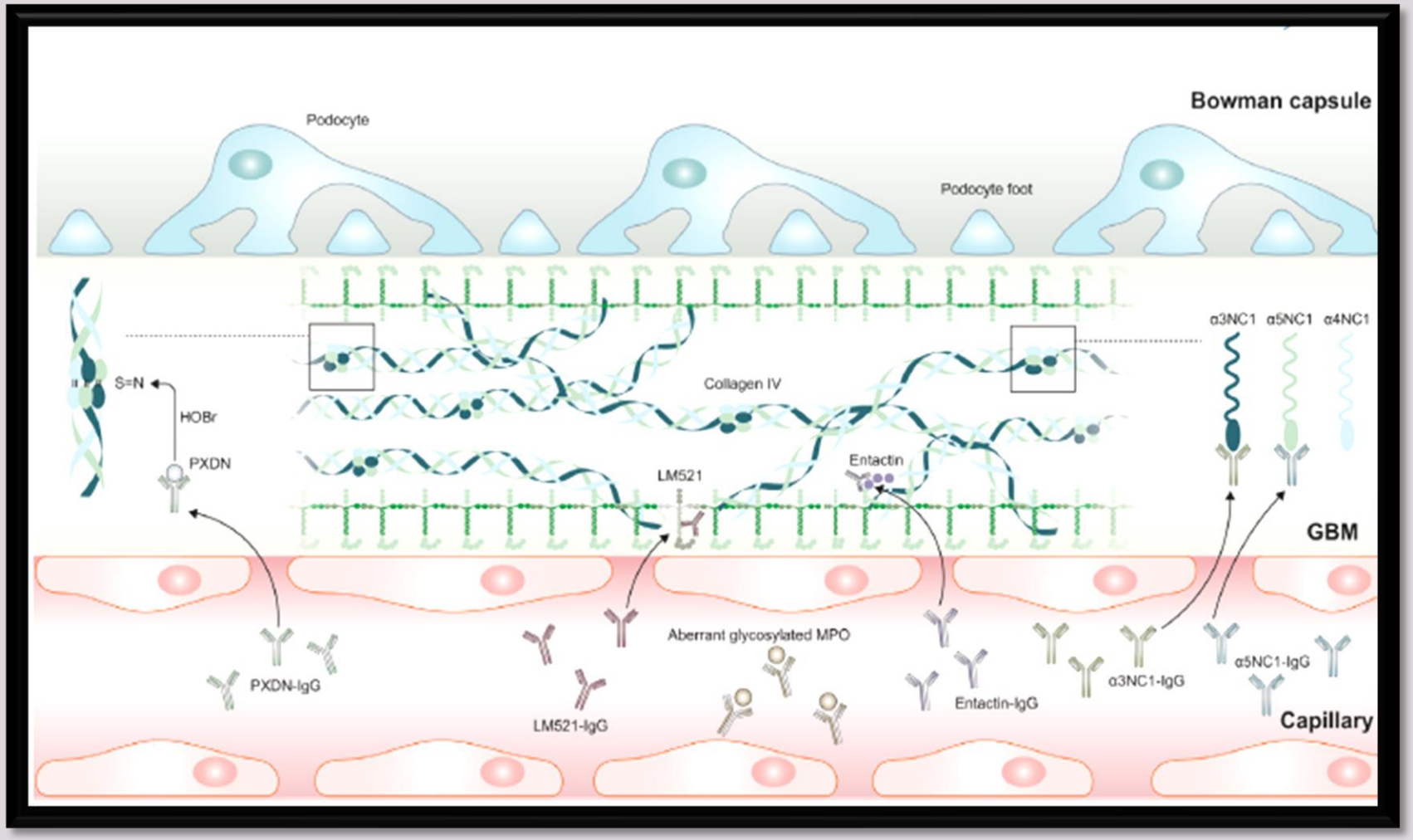
Pathogenesis

Autoantibodies targeting the major GBM components in Anti-GBM Disease



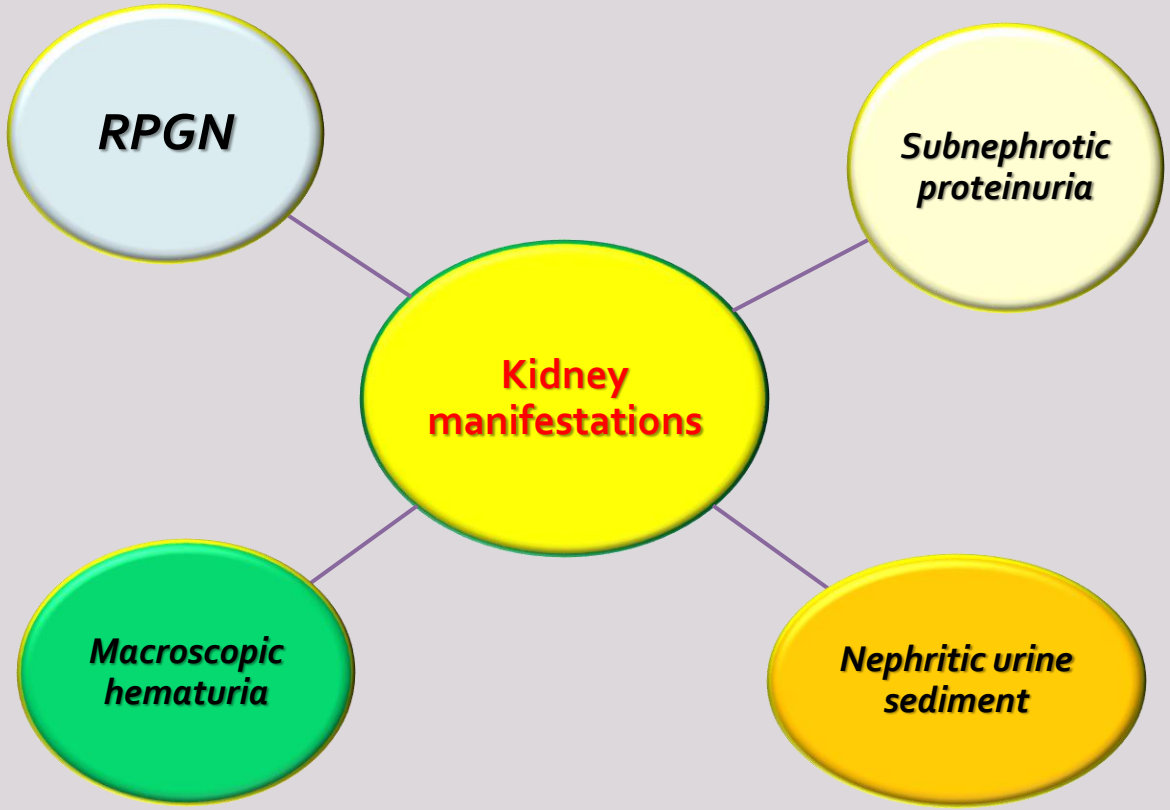
doi: 10.1053/j.ajkd.2022.07.006

Clinical manifestation

- ***typical findings***
- (approximately 90 percent)RPGN
- 25 and 60 percent concomitant alveolar hemorrhage
- small proportion isolated pulmonary findings
- only for a few weeks malaise, weight loss, fever, or arthralgia(Systemic signs and symptoms)
- Serum complement levels are typically within the normal range in patients with anti-GBM disease.

presence of systemic signs and symptoms for a longer period suggests that the patient is double positive for anti-GBM and anti-myeloperoxidase **(MPO-ANCA)** and has features of concurrent vasculitis.

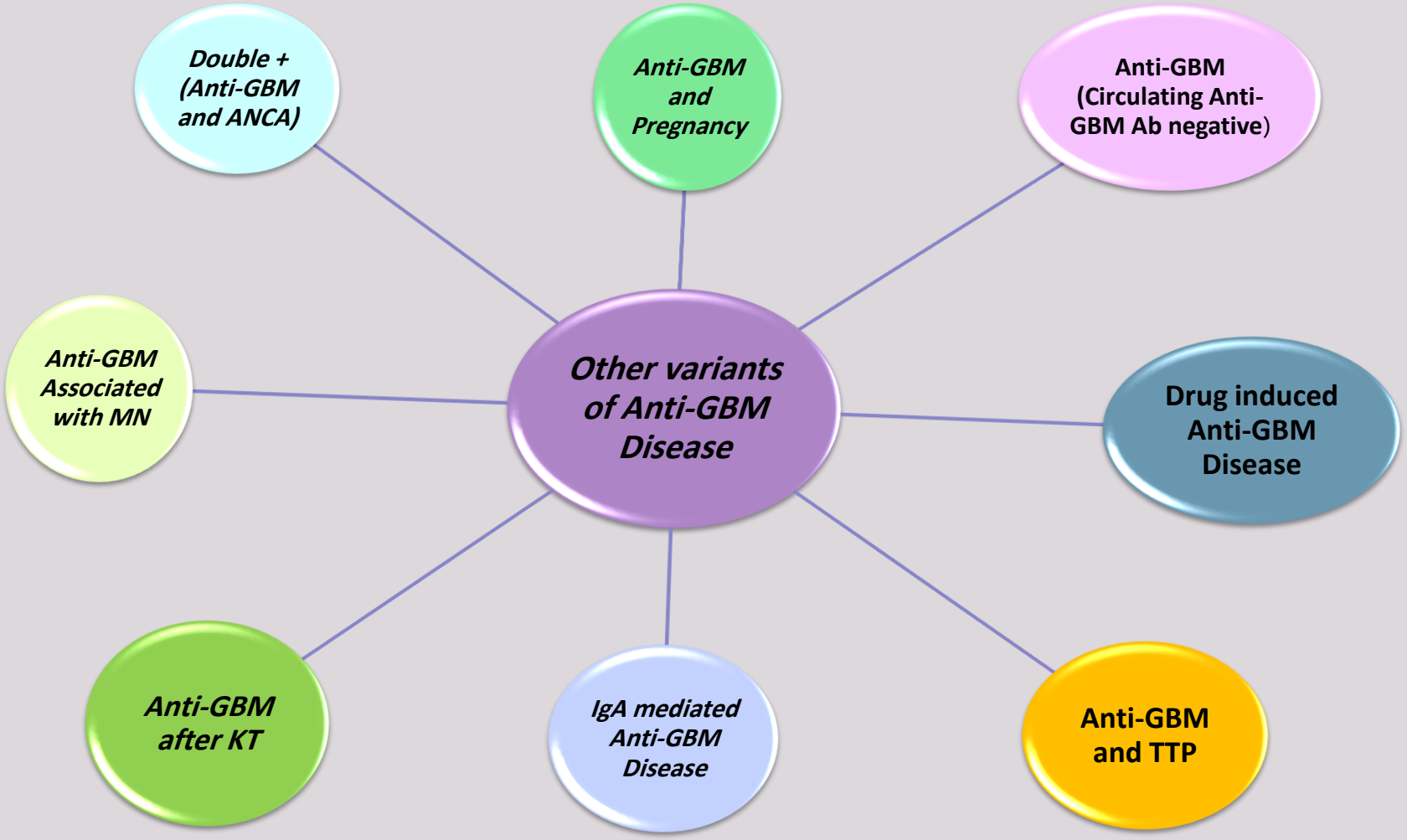
Clinical manifestation



Clinical manifestation

- ***Pulmonary manifestations***
- Alveolar hemorrhage in 25 to 60 percent of patients.
- In rare cases, pulmonary disease predominates .
- Pulmonary manifestations include shortness of breath, cough, sometimes overt hemoptysis, pulmonary infiltrates on chest radiograph, and an increased (DLCO)
- Iron deficiency anemia, possibly due to prolonged pulmonary bleeding

Clinical manifestation



Clinical manifestation

- ***Double-positive anti-GBM and ANCA-associated disease:***
- *~20-40 % of all cases of anti-GBM Disease*
- *Older age and more systemic manifestations than classic anti-GBM disease*
- *Relapse commoner than classic disease*
- *Even if the patient was negative for ANCA on initial testing, ANCA serology should be repeated if there are signs of recurrent disease .*

Clinical manifestation

- ***Anti-GBM disease associated with membranous nephropathy:***
- *The onset of anti-GBM disease may precede, coincide with, or follow the diagnosis of MN.*
- *Serum antibodies against the phospholipase A2 receptor (PLA2R) were undetectable in patients with combined anti-GBM disease with MN.*

Clinical manifestation

- ***Anti-GBM disease without detectable circulating anti-GBM antibodies:***
- ***~5-10 % of all cases of anti-GBM disease have absent circulating anti-GBM Abs.***
- ***Mild clinical and/or histopathological presentation.***

Clinical manifestation

- CTLA4 antagonists
- Anti-PD-1
- alemtuzumab
- Drug-induced anti-GBM disease
- TNF-alpha antagonists
- SARS-CoV-2 Vaccines

Clinical manifestation

Anti-GBM disease after transplantation :

this disorder can occur is 5 to 10 percent of kidney transplants in patients with underlying Alport syndrome (hereditary nephritis) .These patients most commonly have an abnormality in the alpha-5 chain of type IV collagen, although alpha-3 and alpha-4 chain abnormalities may occur.

This leads to defective organization of the alpha-5, -4 and -3 collagen chains in the basement membrane and altered Goodpasture antigen in the alpha-3 chain, so it is not recognized by anti-GBM antibodies.

By comparison, the Goodpasture antigen is normal in the donor kidney, potentially initiating an immune response against this previously "unseen" antigen in the transplanted kidney.

Kidney Biopsy

Evaluation and DX

Pulmonary Studies

Serological Testing

EVALUATION AND DIAGNOSIS

Detection of anti-GBM antibodies, either in serum or histologically, assist in formulating the diagnosis. In approximately 10% of patients with anti-GBM disease circulating antibodies would not be detected.

This may be due to either false negative results within the enzyme immunoassays or due to genuine absence of circulating antibodies, and therefore, histological evidence of disease, through kidney tissue, is important in cases where there remains a high clinical suspicion of disease.

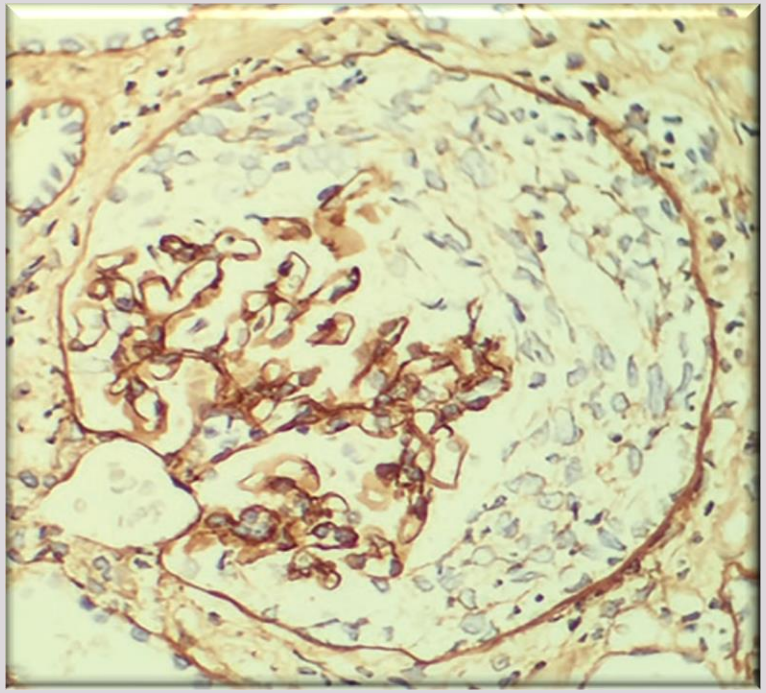
patients with suspected anti-GBM disease should also be tested for ANCA.

EVALUATION AND DIAGNOSIS

kidney biopsy is preferred as this also provides prognostic information that may direct treatment choices, and it can diagnose atypical disease, especially in cases with negative serology. As with all invasive procedures, the risks and benefits must be evaluated, especially in critically unwell patients, as is typically seen in anti-GBM disease.

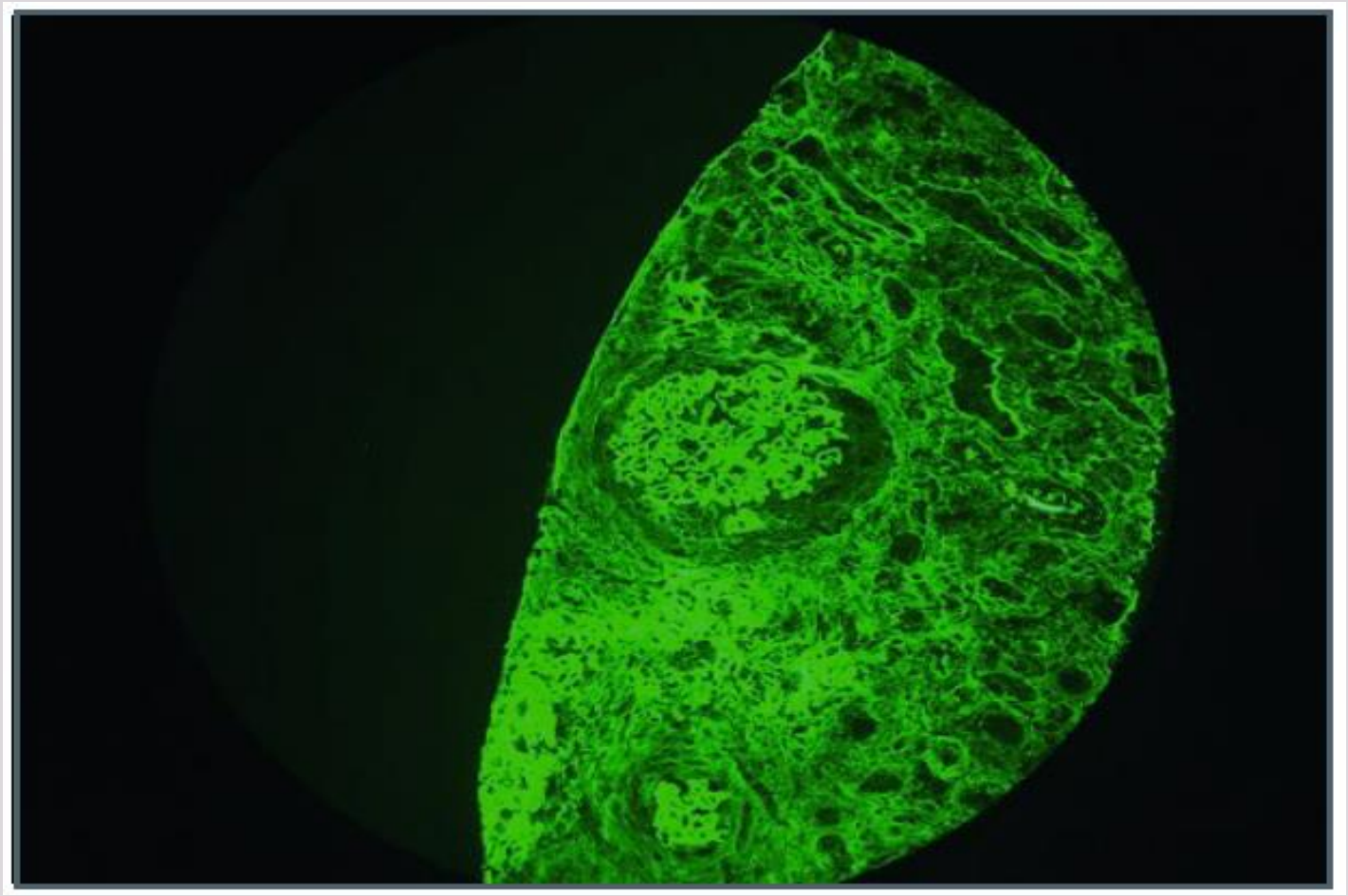
kidney biopsy may be delayed in patients who require urgent treatment for alveolar hemorrhage.

EVALUATION AND DIAGNOSIS



Linear capillary wall positivity for IgG in a glomerulus with a cellular crescent, in a case of anti-GBM disease. X400

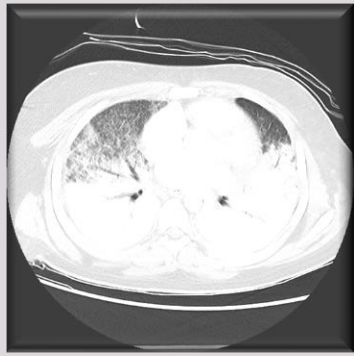
EVALUATION AND DIAGNOSIS



IF microscopy with linear basement staining for IgG and crescentic GN in a patient with Anti-GBM Disease

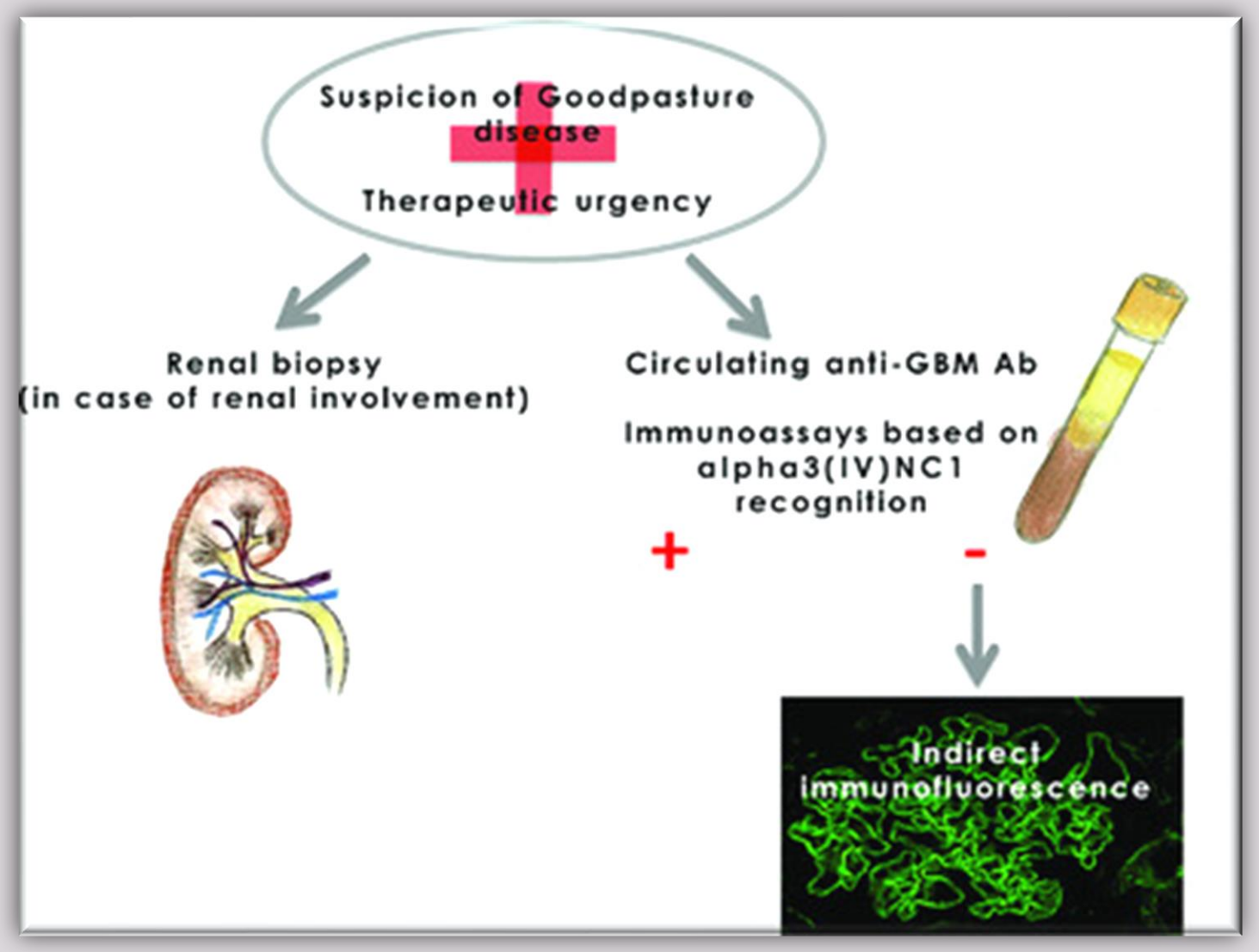
EVALUATION AND DIAGNOSIS

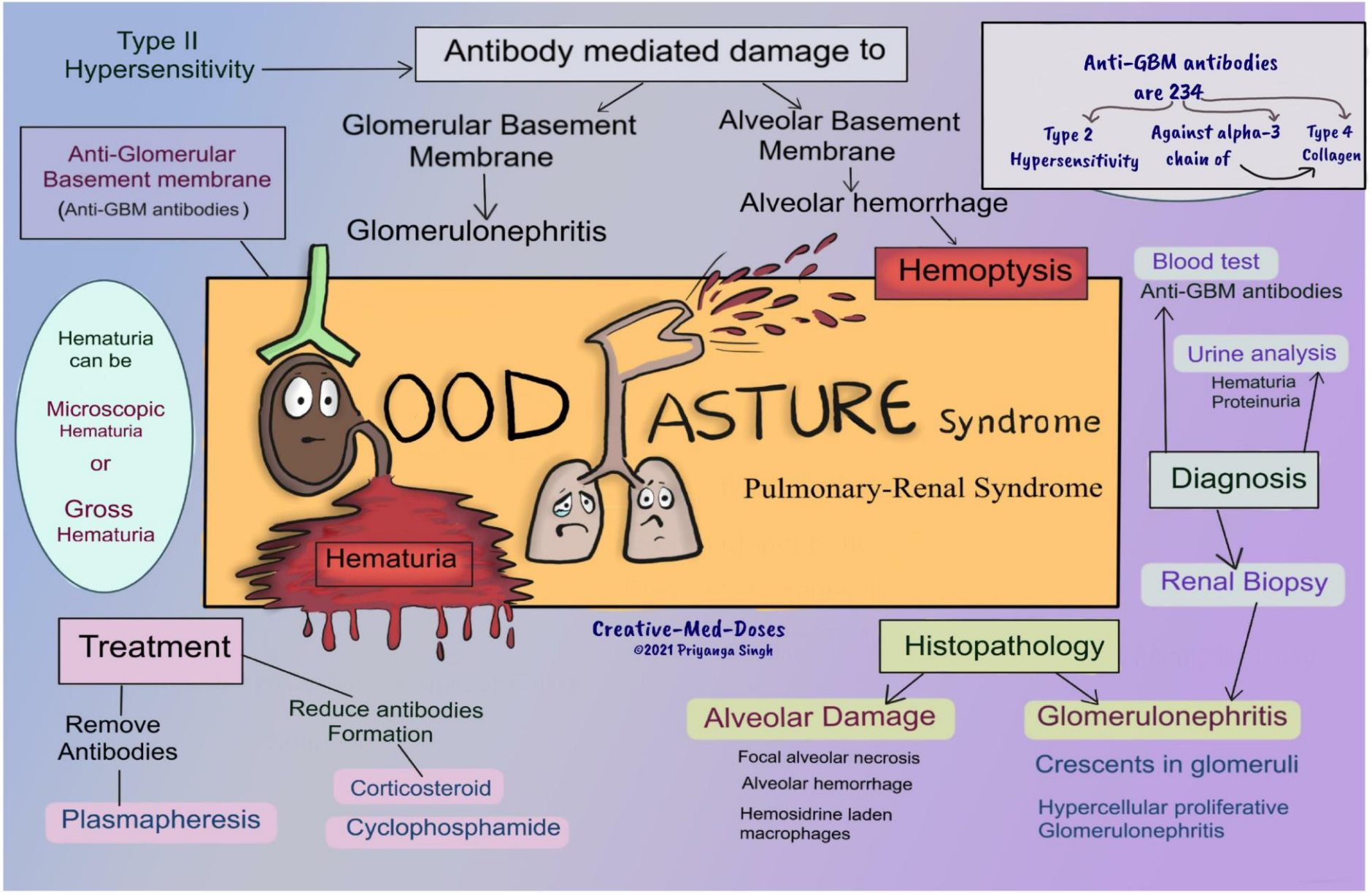
Pulmonary studies are not required to establish the diagnosis of anti-GBM disease; however, a chest radiograph is generally performed in patients who present with recent-onset hemoptysis or dyspnea. Findings on plain chest radiographs in patients with anti-GBM disease and alveolar hemorrhage are nonspecific and typically show new patchy or diffuse opacities.



Further evaluation with high-resolution thoracic computed tomography (CT) scan, which characteristically shows ground glass or consolidative opacities in a diffuse and bilateral distribution, is necessary before pulmonary involvement can be ruled out.

EVALUATION AND DIAGNOSIS




Type II Hypersensitivity
Antibody mediated damage to
Glomerular Basement Membrane
Alveolar Basement Membrane
Anti-GBM antibodies are 234
Type 2 Hypersensitivity
Against alpha-3 chain of
Type 4 Collagen
Anti-Glomerular Basement membrane
(Anti-GBM antibodies)
Glomerulonephritis
Alveolar hemorrhage
Hemoptysis
Blood test
Anti-GBM antibodies
Urine analysis
Hematuria
Proteinuria
Hematuria can be
Microscopic Hematuria
or
Gross Hematuria
GOOD PASTURE Syndrome
Pulmonary-Renal Syndrome
Hematuria
Diagnosis
Renal Biopsy
Creative-Med-Doses
©2021 Priyanga Singh
Treatment
Histopathology
Remove Antibodies
Reduce antibodies Formation
Plasmapheresis
Corticosteroid
Cyclophosphamide
Alveolar Damage
Focal alveolar necrosis
Alveolar hemorrhage
Hemosidrine laden macrophages
Glomerulonephritis
Crescents in glomeruli
Hypercellular proliferative Glomerulonephritis


Anti-GBM Disease

Summary


THANK YOU
for your
ATTENTION!