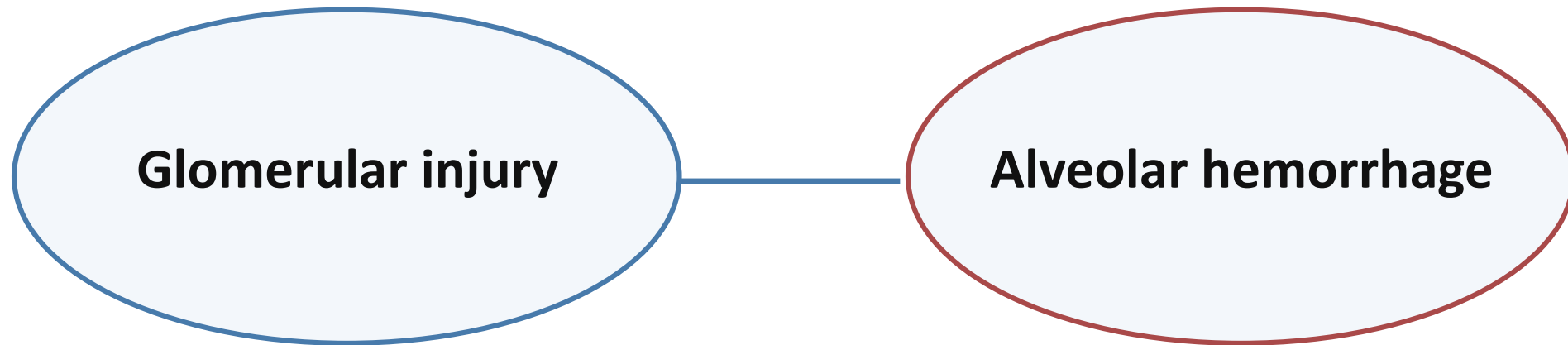


Goodpasture syndrome

Anti-glomerular basement membrane antibody disease
with pulmonary involvement



Shared anti-GBM autoantibodies

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Schematic

Learning objectives

Molecular basis

Anti-GBM antibody specificity

Pathogenesis

Why lung and kidney are injured

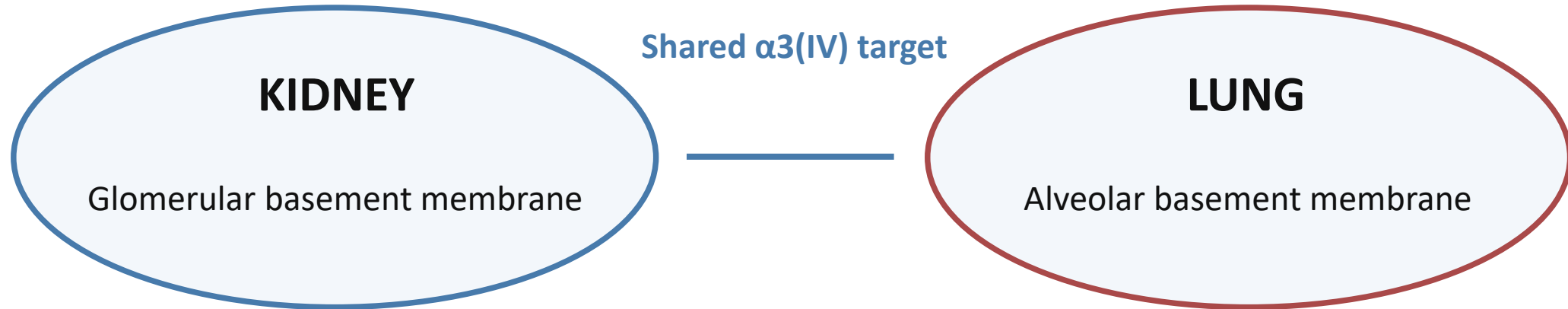
Morphology

Crescents and pulmonary hemorrhage

Clinicopathologic reasoning

Diagnosis, differential and treatment rationale

Goodpasture syndrome: The defining lesion



Schematic — same circulating antibodies can affect both organs

Terminology depends on pulmonary involvement

Renal-limited anti-GBM disease

Anti-GBM antibodies

Renal injury

No pulmonary hemorrhage

Goodpasture syndrome

Anti-GBM antibodies

Renal injury

Pulmonary hemorrhage

Where it sits among pulmonary hemorrhage syndromes

Syndrome	Underlying pattern
Goodpasture	Anti-basement-membrane antibodies
Idiopathic pulmonary hemosiderosis	Unknown cause; anti-GBM antibodies absent
Vasculitis-associated hemorrhage	Inflammatory small-vessel disease

Diffuse pulmonary hemorrhage can reflect several mechanisms • Robbins groups Goodpasture disease, idiopathic hemosiderosis, and vasculitis-associated bleeding

How frequently is the lung involved?

40%–60%

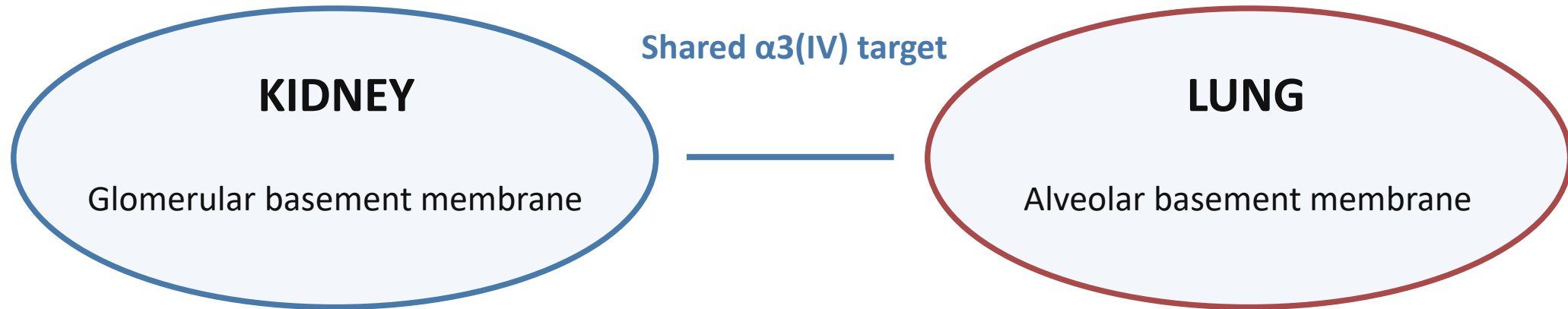
Pulmonary hemorrhage among
patients with anti-GBM antibody
disease

- Pulmonary hemorrhage in 40%–60% of patients with anti-GBM antibody disease
- The remainder are categorized as renal-limited disease
- Pulmonary disease is therefore defining for Goodpasture syndrome, not universal for anti-GBM disease

Epidemiologic profile

- The disease is uncommon and may occur at any age
- Most cases occur in teenagers and people in their twenties
- A male preponderance is described, unlike many autoimmune diseases
- Most patients described are active smokers

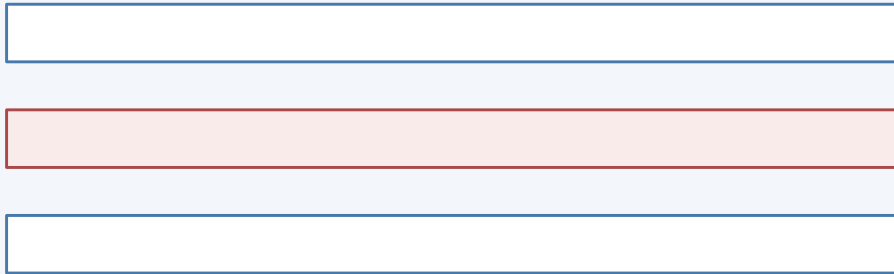
The central pulmonary–renal question



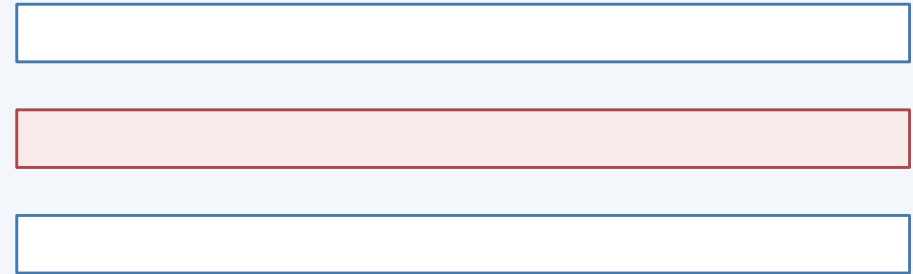
Schematic — same circulating antibodies can affect both organs

Basement membranes: Two vulnerable interfaces

Glomerular filtration barrier



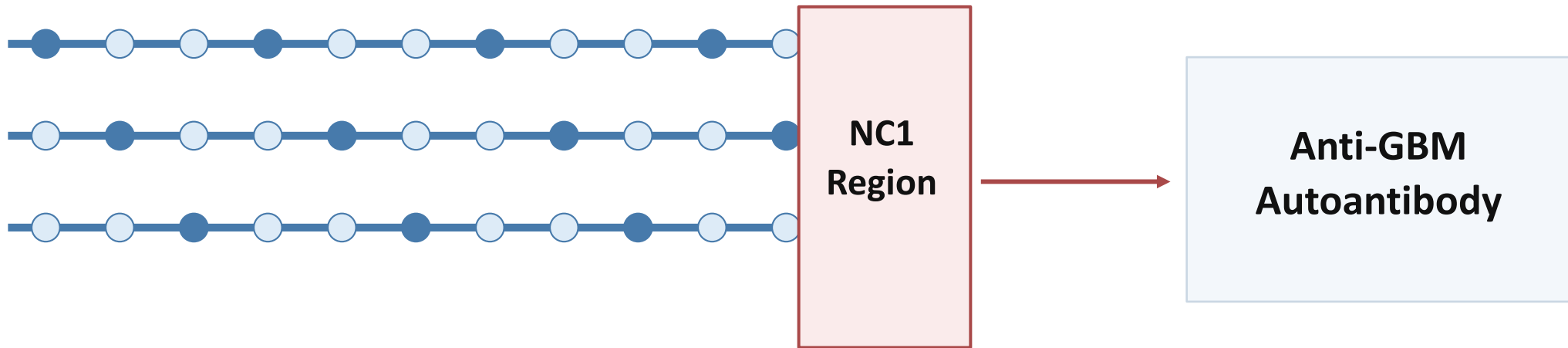
Alveolar air–blood barrier



Shared collagen IV antigen at the basement-membrane layer

The autoantigen is a defined collagen IV domain

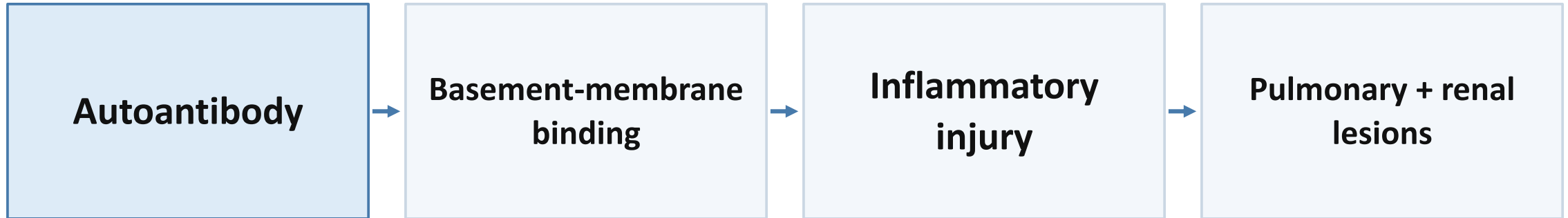
Schematic



Simplified type IV collagen $\alpha 3$ chain antigen concept — not a molecular structure rendering

- Molecular target: Noncollagenous region of collagen type IV $\alpha 3$ chain
- Also present in glomerular and alveolar basement membranes
- The recognition site is not a nonspecific marker of epithelial injury

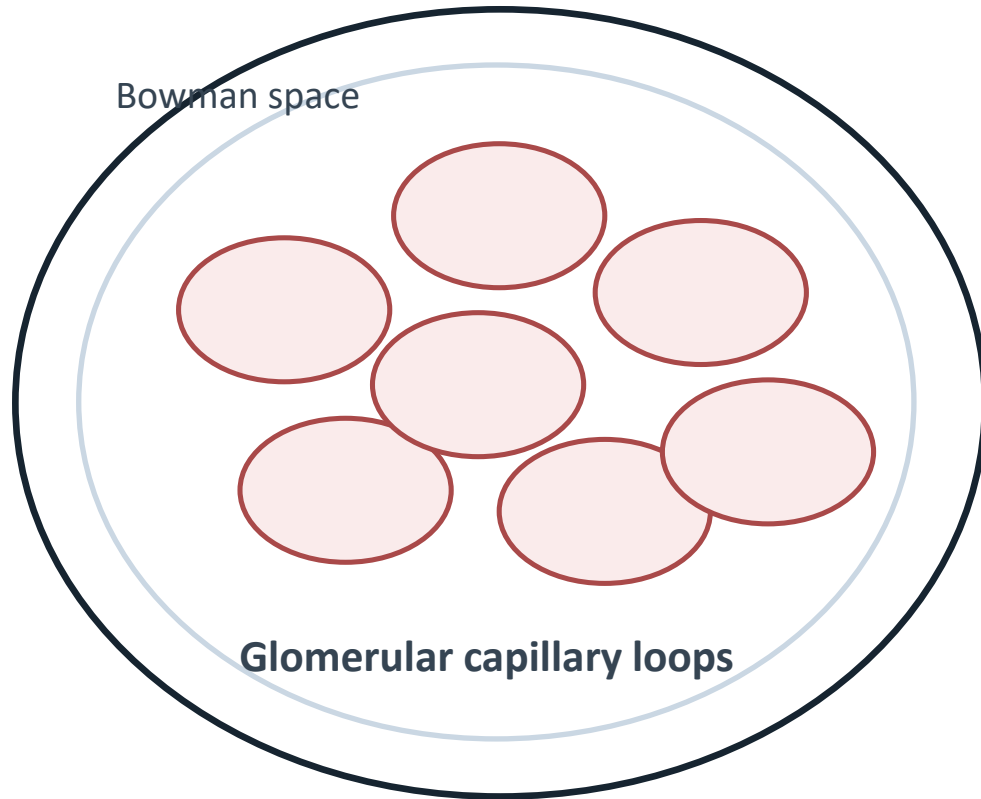
Circulating antibodies initiate tissue injury



- Autoantibodies bind basement-membrane epitopes in target organs
- This initiates inflammation and basement-membrane destruction
- Renal glomeruli and pulmonary alveoli develop different clinical consequences

Renal localization produces glomerulonephritis

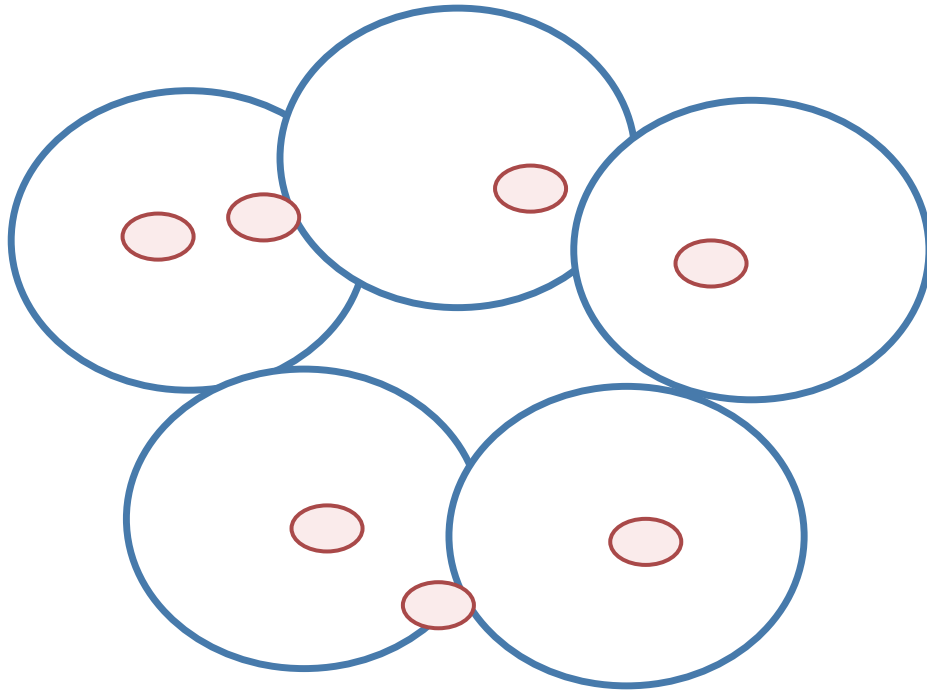
Schematic



- The glomerular basement membrane becomes a site of immune attack
- Inflammatory damage disrupts capillary-wall integrity
- Severe disease progresses to necrosis and extracapillary crescent formation

Pulmonary localization produces alveolar hemorrhage

Schematic



Alveolar airspaces

- Basement-membrane injury involves alveolar septal walls
- Focal septal necrosis permits blood to enter airspaces
- The pathologic lesion is necrotizing hemorrhagic interstitial pneumonitis

One antibody specificity, two injury patterns

Kidney

Glomerular BM injury

Crescentic nephritis

Progressive renal failure

Lung

Alveolar septal injury

Intraalveolar blood

Hemoptysis / consolidations

The initiating trigger remains uncertain

Unknown

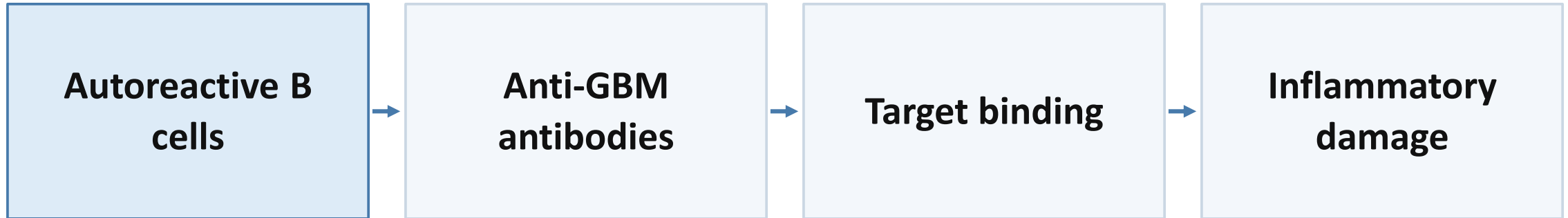
Initiating trigger for autoantibody
formation

- The initiating event that produces anti-GBM autoantibodies is unknown
- Robbins mentions implicated exposures, not established universal causes
- Do not treat association as proof of causation

Genetic susceptibility: HLA association

- Associations include HLA-DRB1*1501 and HLA-DRB1*1502
- These associations are compatible with a predisposition to autoimmunity
- HLA association is not equivalent to a diagnostic genotype

B cells generate the pathogenic antibodies



- Autoreactive B cells are implicated in antibody production
- The circulating antibodies directly bind the target basement membranes
- Removal of circulating antibodies is consequently a therapeutic target

Possible T-cell involvement is qualified

- Experimental data suggest T cells can enhance B-cell function
- T cells may also participate directly in glomerular damage and crescents
- This as supporting evidence, not complete mechanistic resolution

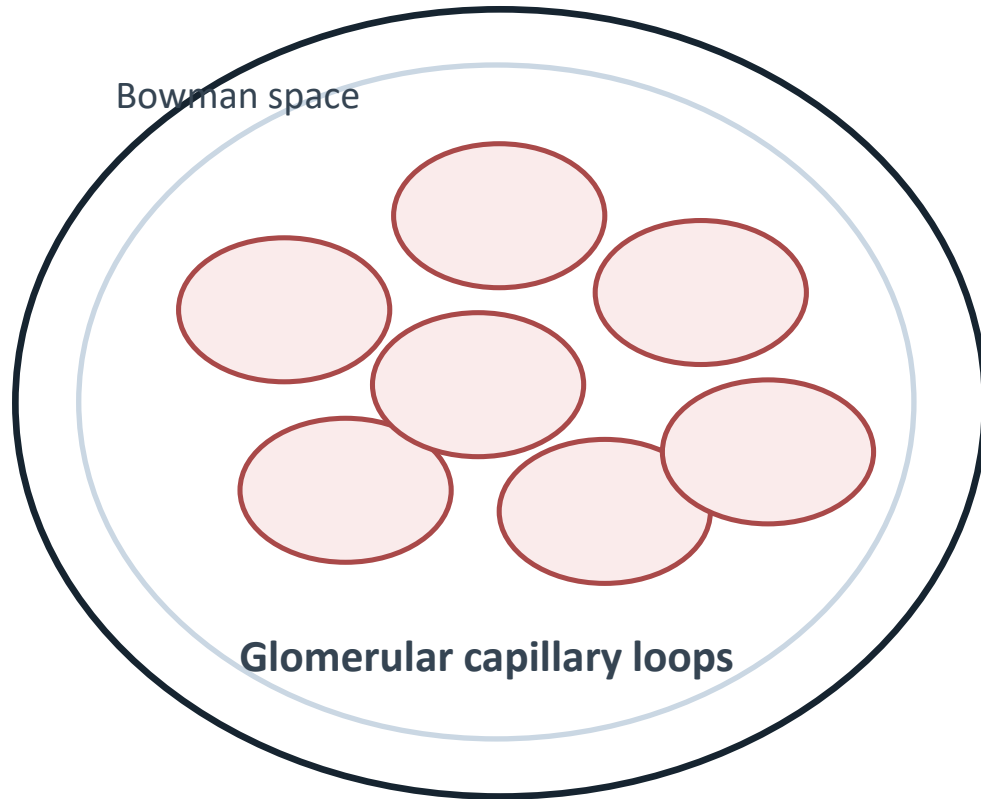
Reported potential exposures are not definitive causes

Reported association	Interpretive status
Viruses	Implicated in some patients
Hydrocarbon solvents	Implicated in some patients
Drugs / cancers	Implicated in some patients
Specific universal trigger	Not established

The textbook implicates viruses, hydrocarbon solvents, certain drugs, and cancers in some patients • Exposure histories may provide context but do not establish causality

Glomerular capillary damage creates urinary-space leakage

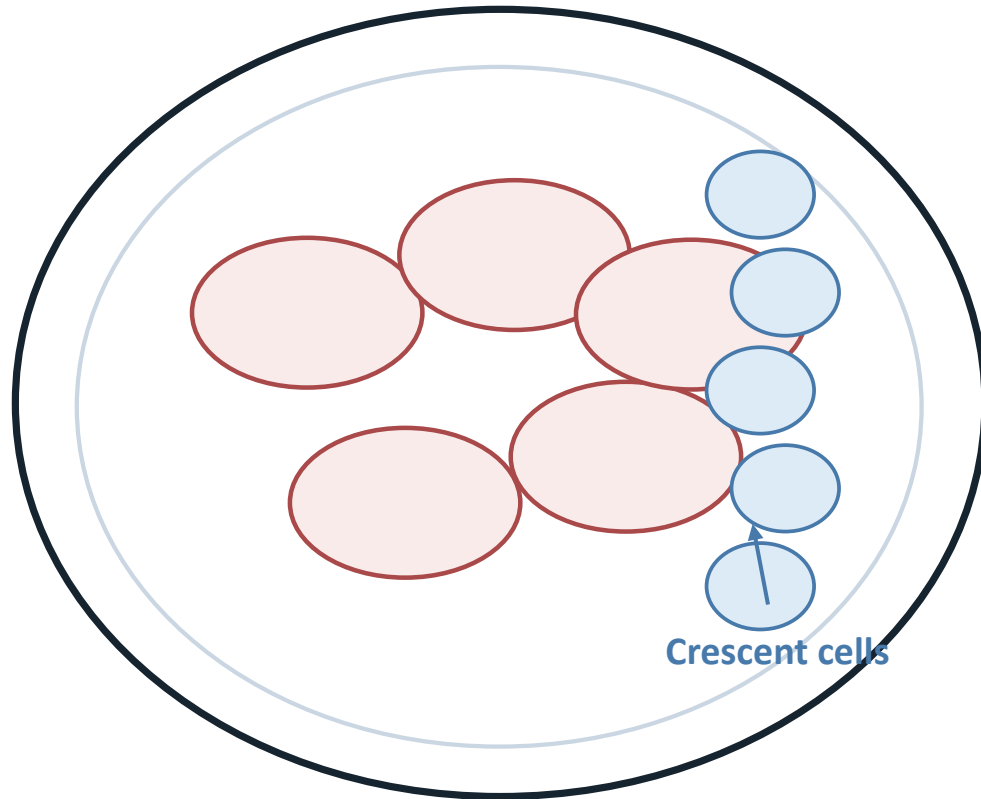
Schematic



- Damaged GBM can develop ruptures in severe crescentic GN
- Plasma proteins, immune mediators, and cells gain access to Bowman space
- This process promotes epithelial and inflammatory-cell crescent formation

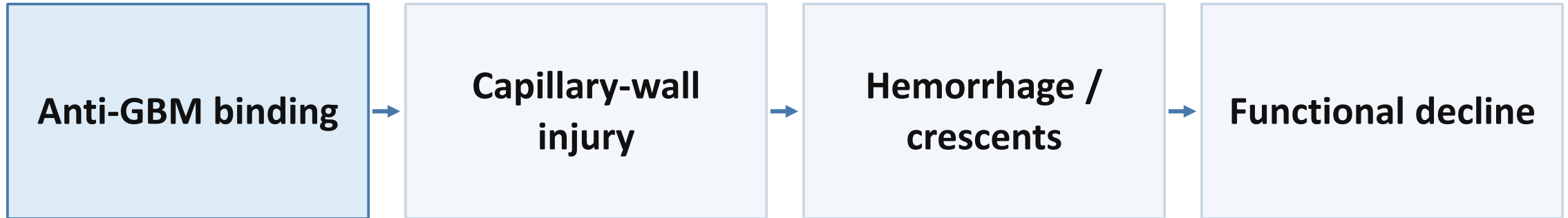
The crescent is a response to severe capillary injury

Schematic



- Crescents form in Bowman space external to the glomerular tuft
- They contain proliferating epithelial cells and inflammatory cells
- Crescents compress the tuft and can obliterate urinary space

A causal map from antibody to organ failure



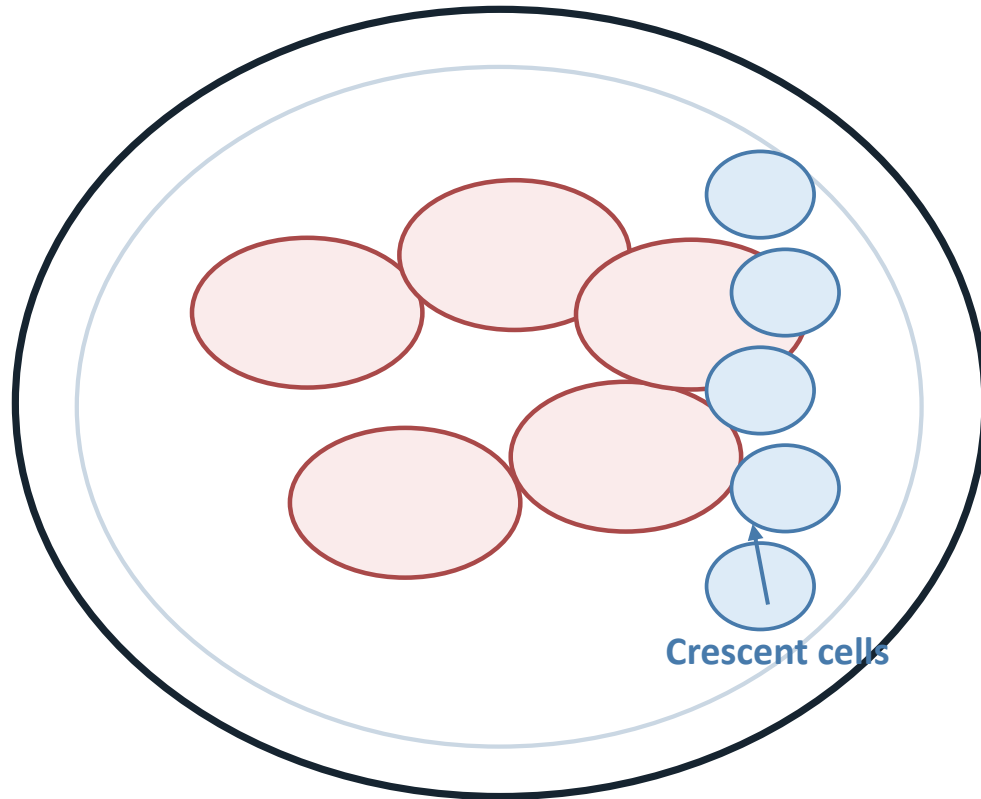
- Linear antibody deposition localizes the immunologic attack
- Capillary-wall injury produces lung hemorrhage and glomerular disruption
- Crescentic glomerulonephritis can evolve rapidly toward renal failure

Kidney involvement may begin focally

- Early cases can show focal proliferative glomerulonephritis
- The morphologic pattern evolves as the antibody-mediated process progresses
- Clinical severity cannot be deduced from the word “focal” alone

Crescentic glomerulonephritis marks severe disease

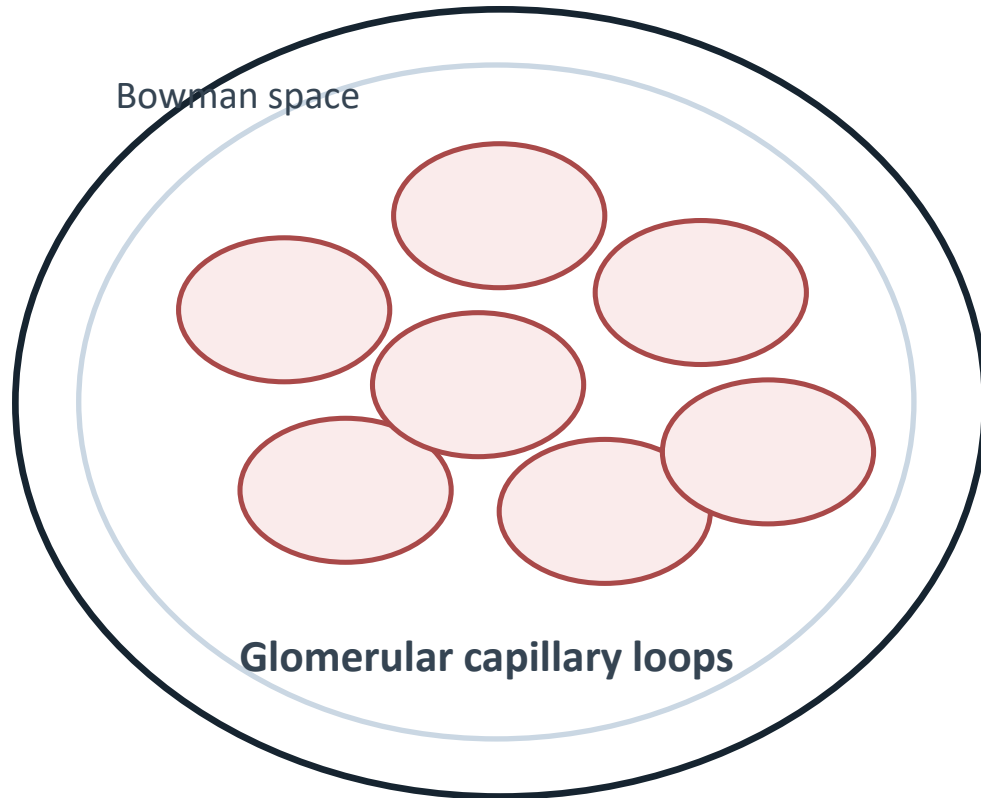
Schematic



- Rapidly progressive GN often shows extracapillary crescents
- Segmental glomerular necrosis and GBM damage may coexist
- Crescents reflect structural injury rather than a specific etiology

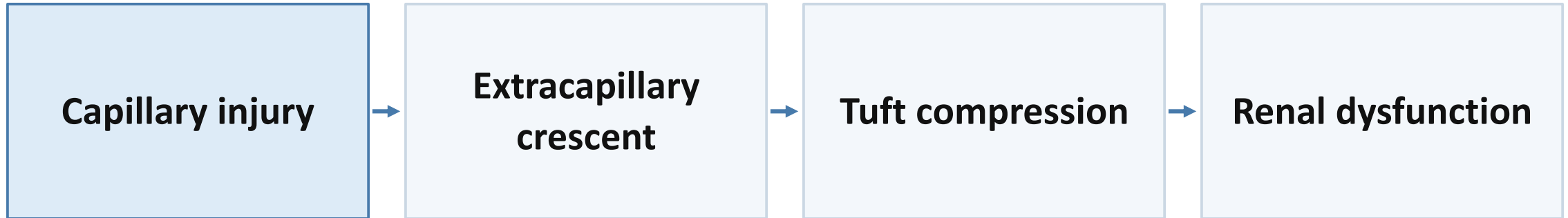
Crescent constituents have diagnostic meaning

Schematic



- Proliferating glomerular epithelial cells line portions of Bowman space
- Monocytes and macrophages accumulate within crescents
- Fibrin may be visible between cellular layers

Why crescents reduce filtration



- Expanding extracapillary cellular tissue compresses the glomerular tuft
- Disrupted glomerular capillaries lose effective filtration surface
- Severe diffuse injury causes rapidly declining renal function

Renal gross changes are not specific

- In crescentic glomerulonephritis, kidneys may be enlarged and pale
- Petechial cortical hemorrhages may be present
- These findings require immunopathologic correlation for etiologic attribution

Renal immunofluorescence is distinctive

Linear GBM staining

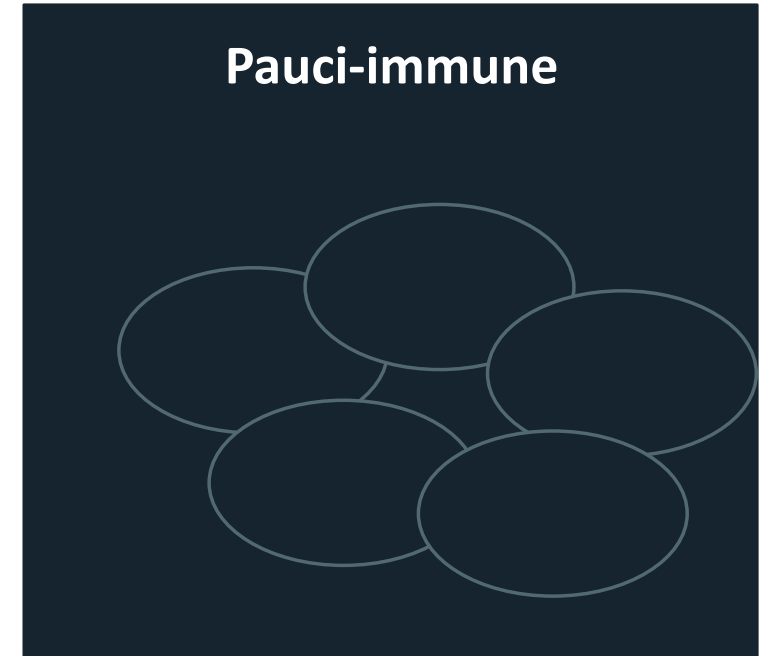
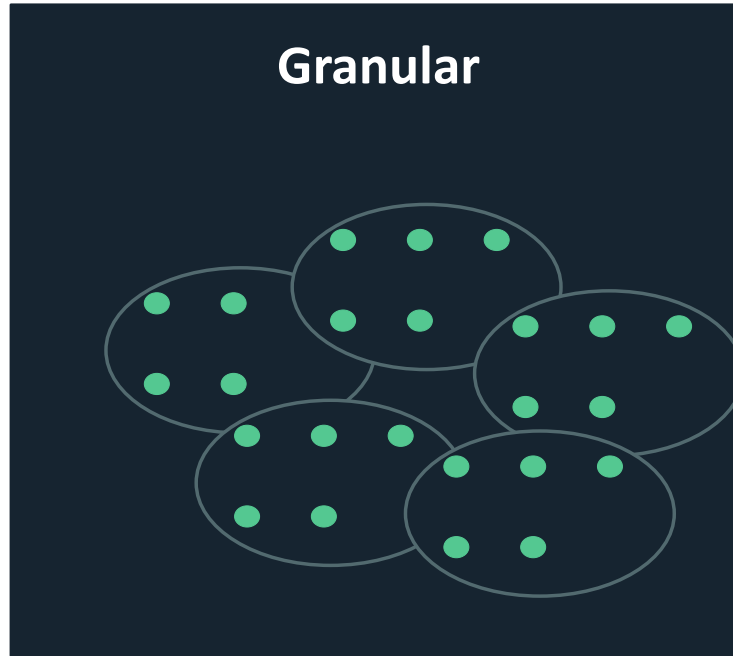
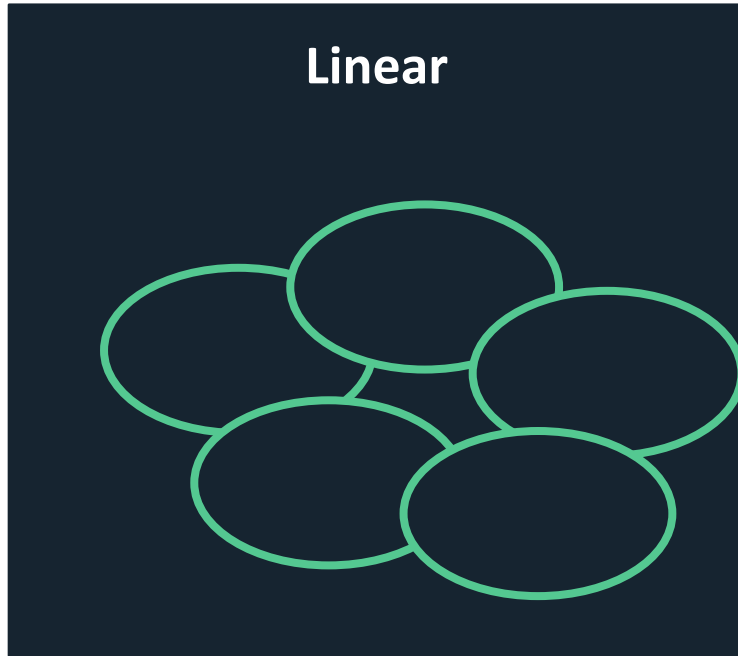


Native schematic

Continuous antibody localization
along a basement-membrane
surface

Schematic immunofluorescence pattern — not a patient biopsy

Linear versus granular immunofluorescence



Schematic immunofluorescence pattern — not a patient biopsy

Three immunopathologic categories of crescentic GN

Category	IF pattern	Illustrative mechanism
Anti-GBM (I)	Linear IgG $\pm$ C3	Basement-membrane antibodies
Immune complex (II)	Granular immune deposits	Immune-complex deposition
Pauci-immune (III)	Little / no deposits	Commonly ANCA-associated

Type I: Anti-GBM antibodies with linear immunofluorescence • Type II: Immune complexes with granular immunofluorescence

Immunofluorescence identifies the disease mechanism



- A crescent is a morphologic reaction and is not etiologically unique
- Linear GBM immune deposits identify an anti-GBM mechanism
- Combine light microscopy, immunofluorescence, and serology for interpretation

Kidney damage can become irreversible



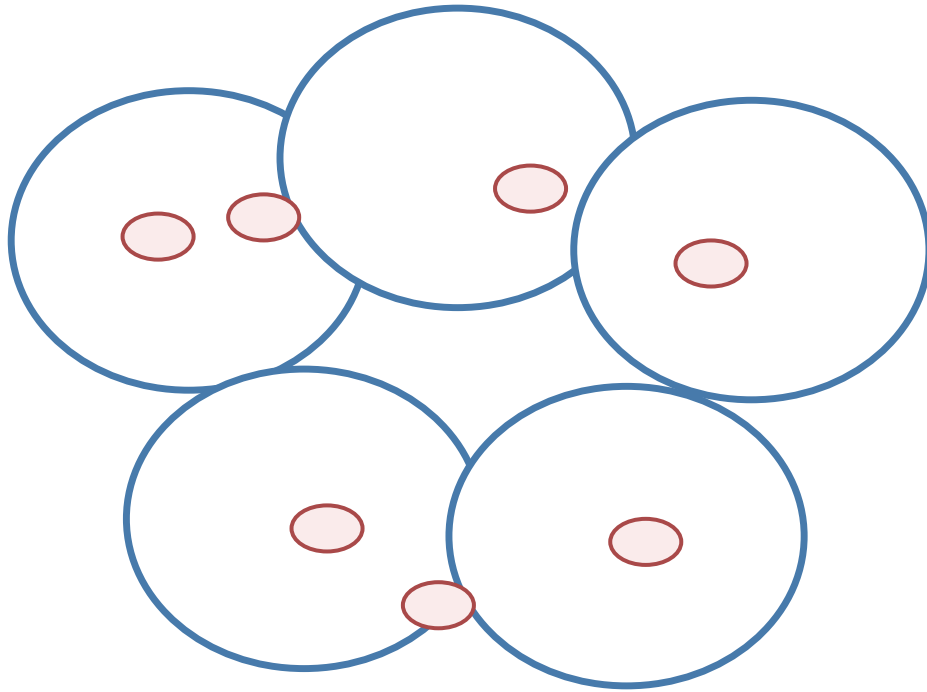
- Crescents may organize and develop a fibrous component over time
- Segmental necrotic lesions may heal with segmental sclerosis
- Early intervention may allow recovery before extensive scarring

Macroscopic lung pathology: Hemorrhagic consolidation

- Classically the lungs are heavy
- Red-brown areas of consolidation may be present
- Gross discoloration corresponds to blood accumulation and breakdown

Alveolar-wall necrosis is the primary lesion

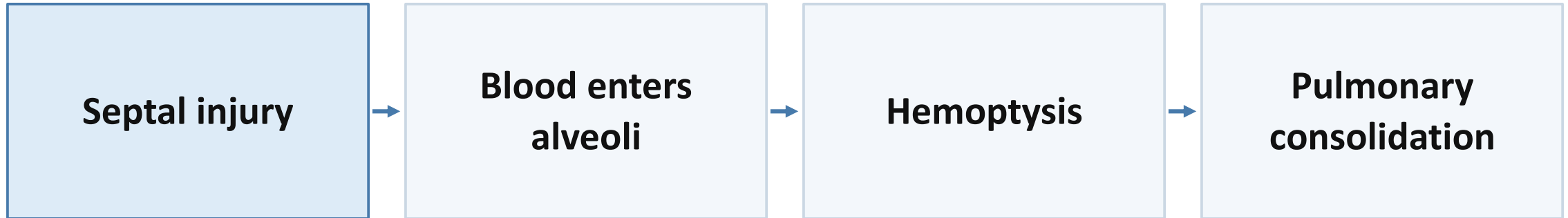
Schematic



Alveolar airspaces

- Histology shows focal necrosis of alveolar septal walls
- Associated hemorrhage fills intraalveolar spaces
- Inflammation and bleeding are linked to capillary basement-membrane injury

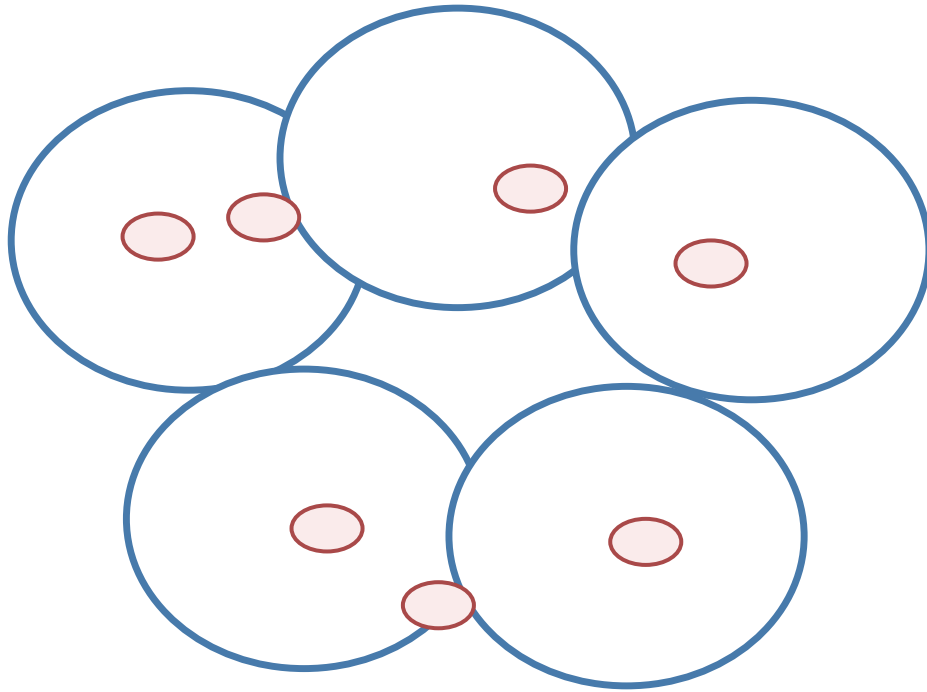
Intraalveolar hemorrhage explains hemoptysis



- Blood entering airspaces may be expelled as hemoptysis
- The same blood can obscure normal aeration on chest imaging
- Pulmonary manifestations may precede overt renal symptoms

Hemosiderin-laden macrophages document prior bleeding

Schematic



Alveolar airspaces

- Alveolar macrophages phagocytose extravasated erythrocytes
- Hemoglobin breakdown produces intracellular hemosiderin
- Repeated or resolving hemorrhage can leave numerous pigmented macrophages

Prussian-blue staining confirms the pigment

H&E examination

Alveolar red cells

Pigmented macrophages

Morphologic hemorrhage

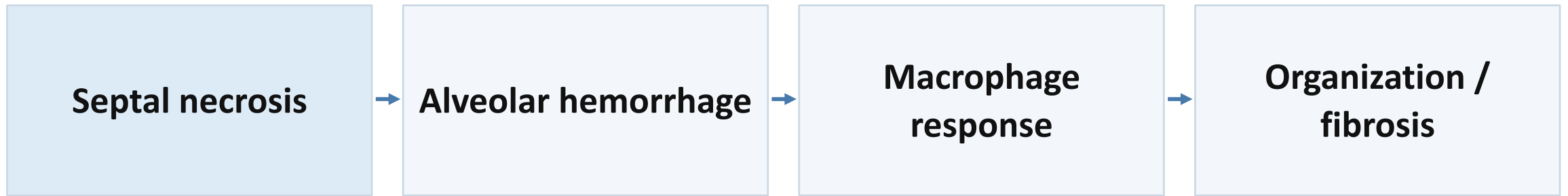
Prussian-blue reaction

Macrophage iron positivity

Confirms hemosiderin

Not etiologically specific

Late pulmonary changes may be organizing



- Fibrous thickening of interalveolar septa can develop
- Type II pneumocyte hyperplasia may appear
- Organization of intraalveolar blood accompanies healing or persistent damage

Pulmonary immunofluorescence may be linear

Linear GBM staining



Native schematic

Continuous antibody localization
along a basement-membrane
surface

Schematic immunofluorescence pattern — not a patient biopsy

What a pulmonary hemorrhage specimen proves



- RBCs and hemosiderin-laden macrophages establish alveolar bleeding
- They do not alone identify an anti-GBM cause
- Renal immunopathology and anti-GBM serology supply mechanistic specificity

Kidney and lung: Integrated morphology

Renal compartment

Glomerular capillary wall

Crescents / renal failure

Linear GBM deposits

Pulmonary compartment

Alveolar septal wall

Alveolar hemorrhage

Sometimes linear septal deposits

Pulmonary pathology differential is wide

Cause group	Clue to mechanism
Anti-GBM	Linear GBM deposits / anti-GBM antibodies
Idiopathic hemosiderosis	Anti-GBM antibodies absent
Vasculitis-associated	Clinical / pathologic vasculitis features

Alveolar hemorrhage is a shared pathologic pattern • Vasculitides and idiopathic hemosiderosis also produce alveolar bleeding

Clinical presentation often starts in the lung



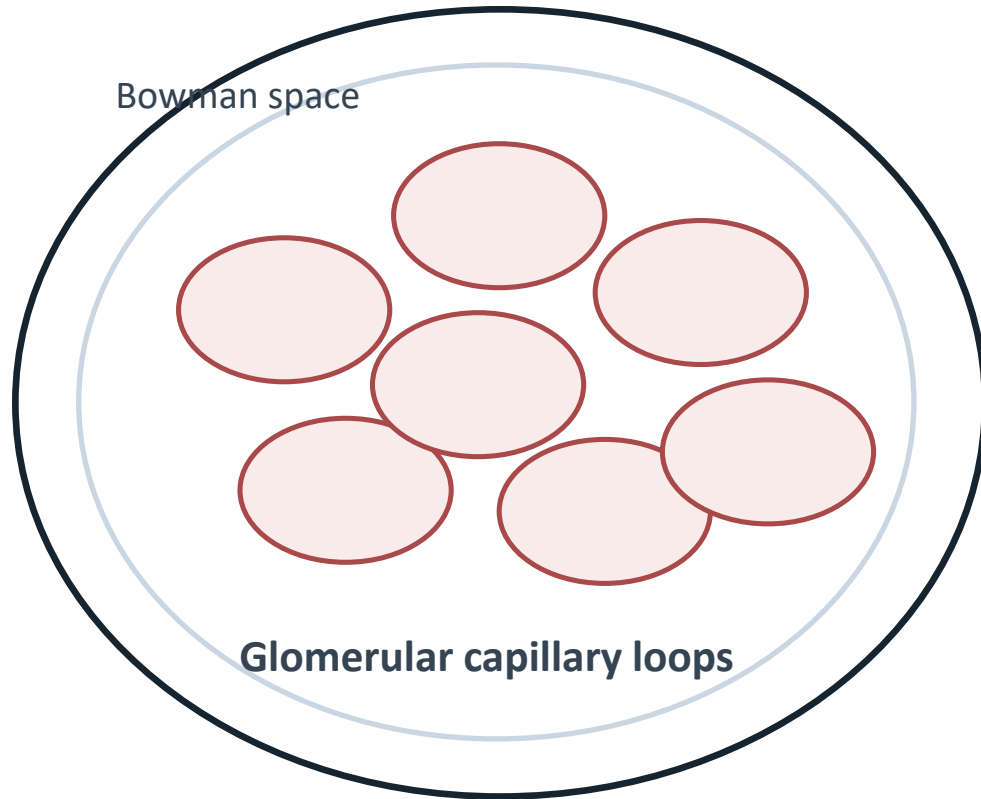
- Respiratory symptoms as the initial presentation in most cases
- Hemoptysis is a principal symptom
- Chest imaging may show focal pulmonary consolidations

Pulmonary hemorrhage may be life-threatening

- Recurrent hemoptysis may dominate the clinical course
- Severe bleeding can compromise respiratory function
- Do not dismiss ongoing alveolar hemorrhage because renal symptoms are initially subtle

Nephritic urine abnormalities indicate glomerular injury

Schematic



- Hematuria and red blood cell casts characterize the renal syndrome
- Proteinuria accompanies damaged glomerular filtration barriers
- Correlate urine findings with evolving renal functional impairment

Other renal manifestations follow capillary injury

- Blood pressure may be elevated
- Edema can accompany impaired renal function
- Proteinuria is usually moderate but may occasionally reach nephrotic range

Rapidly progressive renal dysfunction is characteristic



- Renal decline often evolves over weeks
- Severe oliguria may develop
- The syndrome can advance to severe renal failure if treatment is delayed

Uremia was historically a major cause of death

- Uremia as the most common cause of death
- This emphasizes the clinical severity of glomerular injury
- Treatment has substantially improved outcomes compared with historical prognosis

Recognizing the pulmonary–renal syndrome



- Hemoptysis plus glomerular hematuria suggests a shared systemic process
- A rapidly falling renal function warrants urgent mechanistic evaluation
- Goodpasture syndrome is one important cause, not the sole cause

Initial diagnostic evidence must be integrated



- Serum anti-GBM antibody measurement helps identify the cause
- Urinalysis and renal-function testing define the nephritic phenotype
- Biopsy and immunofluorescence establish the tissue injury pattern

Serologic classification avoids single-test reasoning

Investigation	Interpretive role
Serum anti-GBM antibodies	Supports anti-GBM mechanism
ANCA	Evaluates pauci-immune vasculitis
ANA	Assesses immune-complex / autoimmune alternatives
Renal IF	Distinguishes linear / granular / pauci patterns

Anti-GBM antibodies identify an antibody-mediated possibility • ANCA and antinuclear antibody testing assist differential diagnosis

Idiopathic pulmonary hemosiderosis differs mechanistically

Goodpasture syndrome

Anti-GBM antibodies

Renal glomerular injury

Pulmonary hemorrhage

Idiopathic hemosiderosis

Antibodies undetectable

Unknown mechanism

Intermittent alveolar hemorrhage

Granulomatosis with polyangiitis is another comparator

Anti-GBM disease

Antibody to collagen IV $\alpha 3$

Linear renal IF

Pulmonary hemorrhage

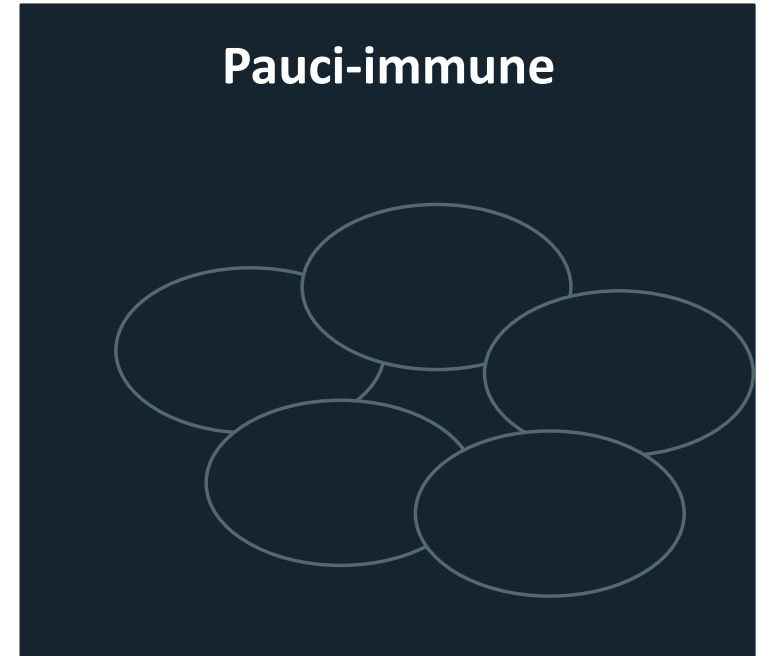
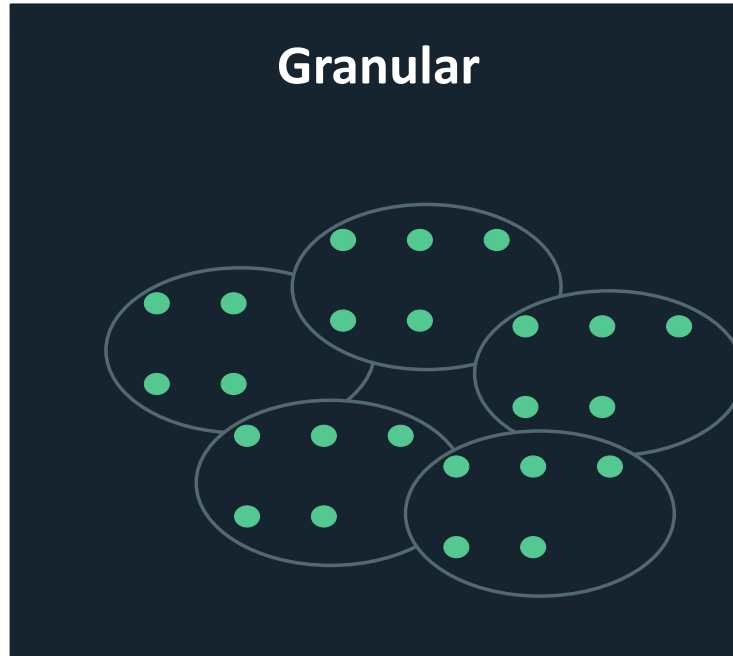
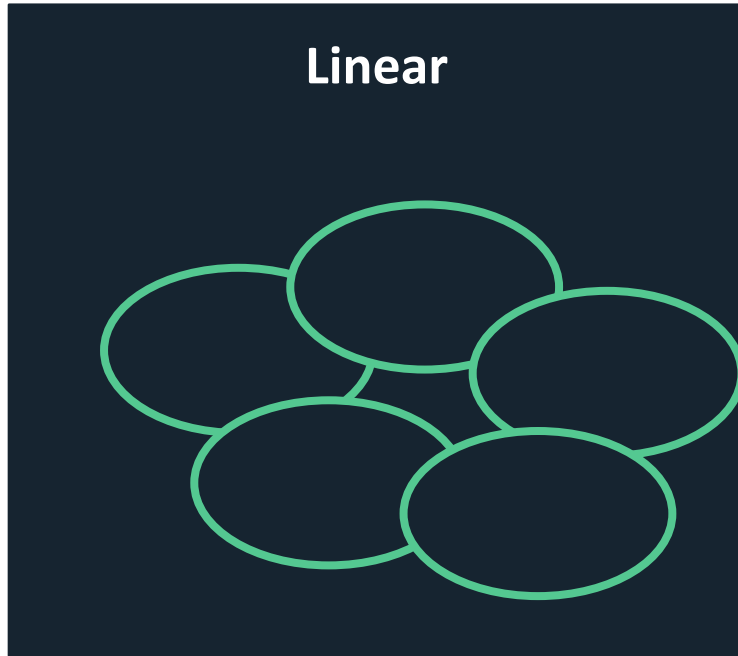
GPA

Vasculitis-associated injury

Capillaritis / granulomas

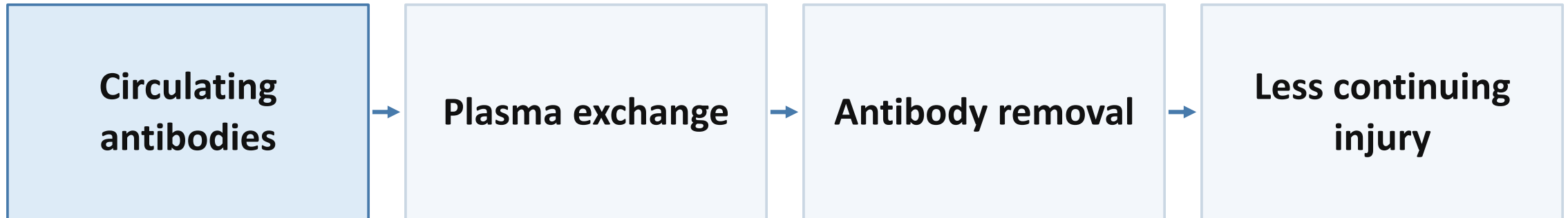
May cause pulmonary hemorrhage

Renal IF is a high-yield diagnostic discriminator



Schematic immunofluorescence pattern — not a patient biopsy

Why plasma exchange is mechanistically rational



- Plasma exchange removes circulating pathogenic anti-GBM antibodies
- It may also remove other soluble mediators of injury
- The objective is to reduce continuing basement-membrane attack

Why immunosuppression must accompany exchange

Plasma exchange

Removes circulating antibody

Reduces immediate antibody load

Addresses existing mediator

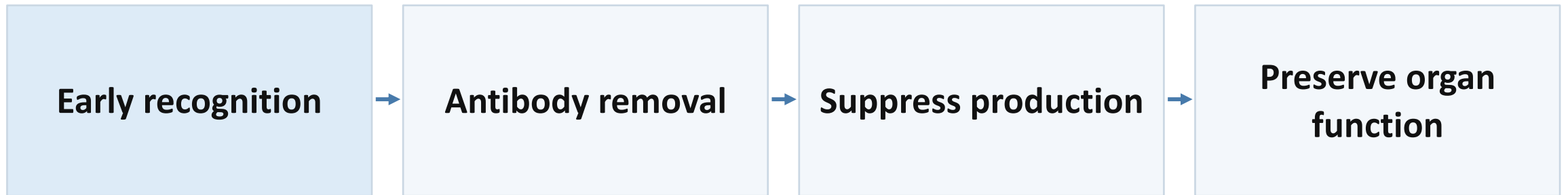
Immunosuppression

Suppresses new production

Reduces ongoing immune attack

Addresses immune source

Early treatment matters for renal recovery



- Early plasma exchange with steroids and cytotoxic therapy may allow renal recovery
- Pulmonary hemorrhage may improve with suppression of the immune process
- Advanced scarring and late presentation limit the prospect of recovery

Case: Hemoptysis followed by nephritic urine

- A young adult develops hemoptysis and new urinary red blood cell casts
- Renal function deteriorates over the following weeks
- What mechanism unifies the pulmonary and renal findings?

What mechanism or diagnosis best explains the pattern?

Case interpretation: The decisive histologic pattern

- Kidney biopsy shows crescents and continuous linear IgG along GBM
- A crescent alone would not identify the cause
- Linear immunofluorescence supports anti-GBM crescentic GN

Diagnostic distinction: Linear GBM staining identifies anti-GBM injury; Crescents indicate severity.

Case: Hemorrhage with negative anti-GBM antibodies

- A child has intermittent diffuse alveolar hemorrhage and anemia
- Anti-basement membrane antibodies are undetectable
- Why is idiopathic pulmonary hemosiderosis a competing diagnosis?

What mechanism or diagnosis best explains the pattern?

Case: Crescentic GN with granular deposits

- The biopsy shows crescents, but IF has granular Ig and complement deposits
- Which classification does that pattern favor?
- What conclusion should not be drawn from crescents alone?

What mechanism or diagnosis best explains the pattern?

Three diagnostic pitfalls

Pitfall	Corrective principle
Alveolar hemorrhage = Goodpasture	Different causes share the same lung pattern
Any crescent = anti-GBM	Classify by renal IF and serology
Suspected exposure = cause	Trigger remains uncertain

Equating all alveolar hemorrhage with Goodpasture syndrome • Treating all crescentic glomerulonephritis as anti-GBM disease

Concept synthesis: Evidence at three levels

MOLECULAR

Antibody to collagen IV α 3 noncollagenous domain

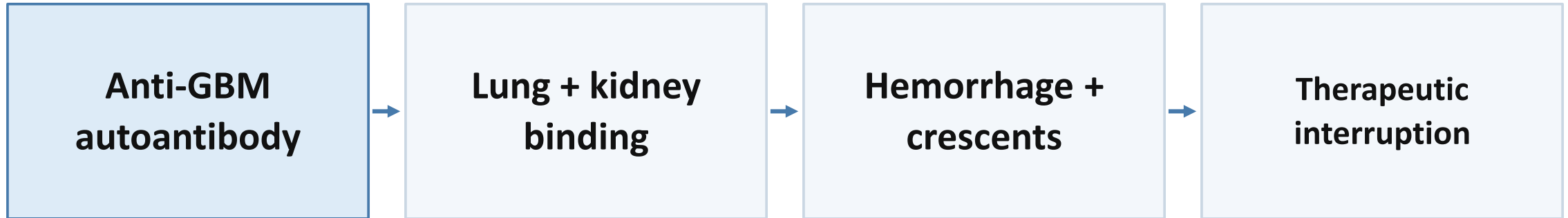
MORPHOLOGIC

Glomerular crescents, linear GBM deposits, alveolar hemorrhage

CLINICAL

Hemoptysis plus rapidly progressive nephritic renal disease

The disease in one causal sequence



- Autoantibody formation → shared basement-membrane targeting
- Inflammatory capillary injury → lung hemorrhage and glomerular damage
- Plasma exchange plus immunosuppression interrupts ongoing immune injury

High-yield diagnostic checklist

- Pulmonary evidence: Hemoptysis / infiltrates / alveolar hemorrhage
- Renal evidence: Hematuria, RBC casts, renal decline
- Mechanistic evidence: Anti-GBM antibodies and linear GBM immunofluorescence
- Differentiate immune-complex and pauci-immune processes

Suggested reading

- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th edition.
- The Lung: diffuse pulmonary hemorrhage and Goodpasture syndrome.
- The Kidney: anti-GBM disease and crescentic glomerulonephritis.
- Detailed source location and diagram provenance are provided in instructor notes.