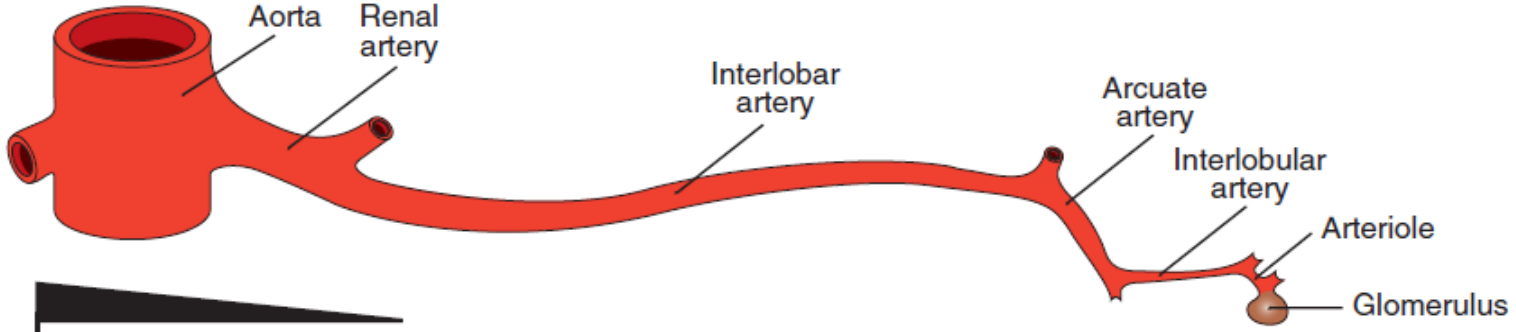
Renal Vasculitis

- Definition & Introduction:
  - Kidney has a large number & variety of renal vessels.
  - Kidneys are targets of a variety of systemic vasculitides especially of small vessels
  - Vasculitides are classified into:
    - Large-vessel vasculitis
    - Medium-sized vessel vasculitis
    - Large-vessel vasculitis



- Large-vessel vasculitis
  - Granulomatous arteritis in a patient >50 years
    - Giant cell arteritis
  - Granulomatous arteritis in a patient <50 years
    - Takayasu arteritis
- Medium vessel vasculitis
  - Necrotizing arteritis without mucocutaneous lymph node (MCLN) syndrome
    - Polyarteritis nodosa
  - Necrotizing arteritis with MCLN syndrome
    - Kawasaki disease
- Small-vessel vasculitis
  - Immune complexes in vessel walls with immunofluorescent (IF) staining for immunoglobulins
    - Other sources for immune complexes
      - Other immune complex vasculitis
    - Cryoglobulins in blood and vessel walls
      - Cryoglobulinemic vasculitis
    - IgA-dominant deposits in vessel walls
      - IgA vasculitis (HSP)
    - Systemic lupus erythematosus or rheumatoid arthritis
      - Lupus/rheumatoid vasculitis
  - Circulating antineutrophil cytoplasmic antibodies (ANCA) with paucity of vascular immunoglobulin staining
    - No asthma or granulomas
      - Microscopic polyangiitis
    - Granulomas and no asthma
      - GPA (Wegener)
    - Eosinophilia, asthma, and granulomas
      - EGPA (Churg-Strauss)

- Clinical manifestations depend on the type of renal vessel affected

1. Small vessel vasculitis:
   - Affects vessels smaller than arteries (capillaries, venules & arterioles)
   - Most common target is the glomeruli ---- GN
2. Medium-vessel vasculitis:
   - Mostly affecting interlobar & arcuate arteries --- Renal infarction or hge
3. Large-vessel vasculitis:
   - Mostly affecting aorta (renal ostia) & its major branches (main renal artery) ---- RVH

Small-Vessel Pauci-Immune Vasculitis

- Definition:

- Absence or paucity of immune complexe deposits in vessel walls
- Affects capillaries, venules, arterioles & small arteries:
  - Glomerular capillaries ---- GN
  - Pulmonary alveolar capillries --- Alveolar he
  - Dermal venules ---- Purpura

- They include:

1. Microscopic polyangitis

2. *Granulomatosis with polyangiitis* (Wegener) (GPA) :

   Small-vessel vasculitis + necrotizing granulomatous inflammation (Respiratory tract)

- 3. *Eosinophilic granulomatosis with polyangiitis* (Churg-Strauss) (EGPA) :

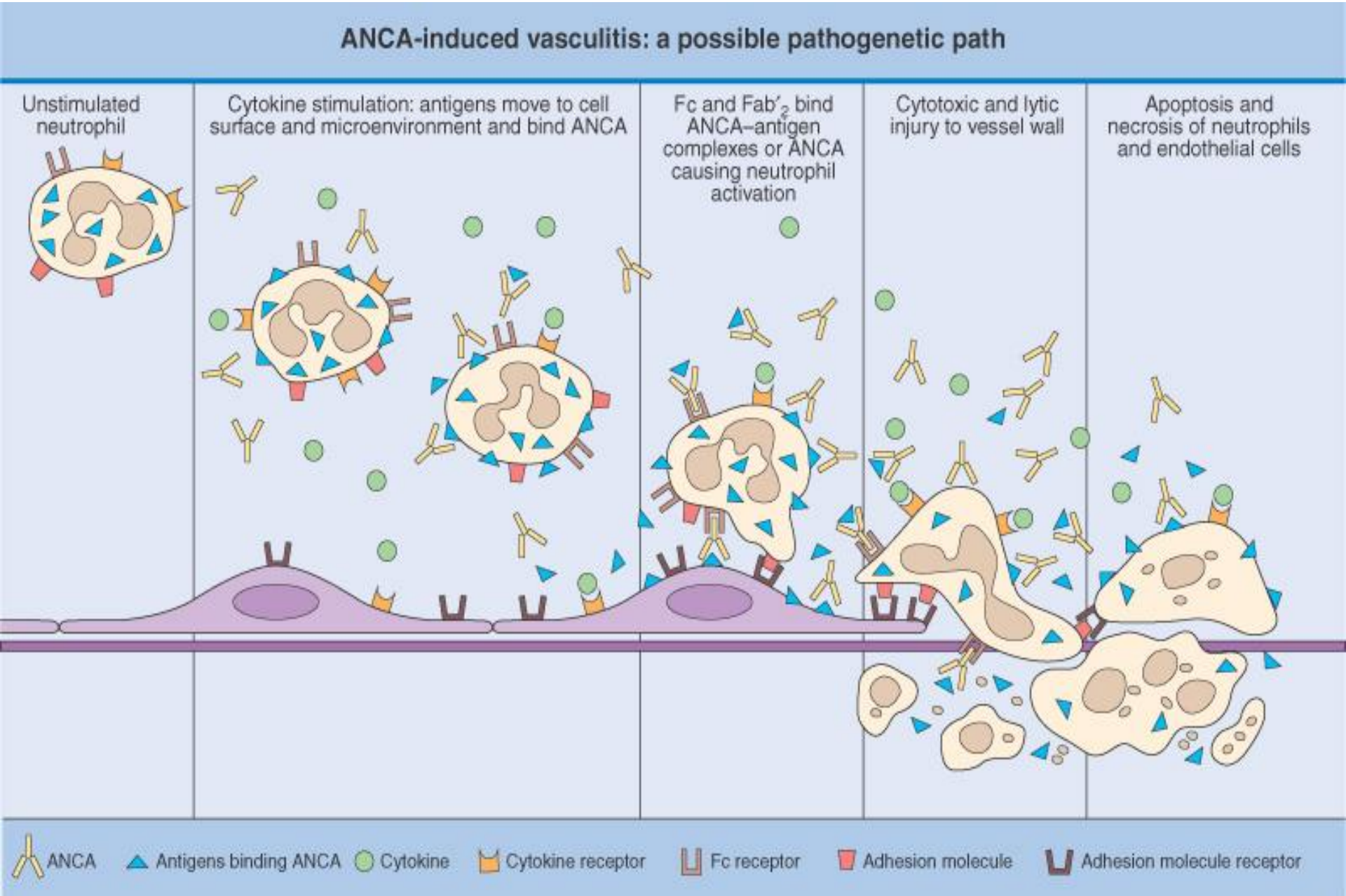
  Small-vessel vasculitis + necrotizing granulomatous inflammation (Respiratory tract)

  Asthma & eosinophilia

4. Renal-limited vasculitis or idiopathic RPGN

- All of them can produce pauci-immune crescentic GN

- Pathogenesis:



- Epidemiology:

- 5th, 6th & 7th decades
- Male ≥ Female
- Caucasions > African Americans
- Europe:
  - Microscopic polyangitis: 2.5/100,000
  - GPA: 2.5/100,000
  - EGPA: 1/100,000

Clinical Manifestations

1. **Constituti** ia, myalgia & arthralg

2. **Renal (MP**

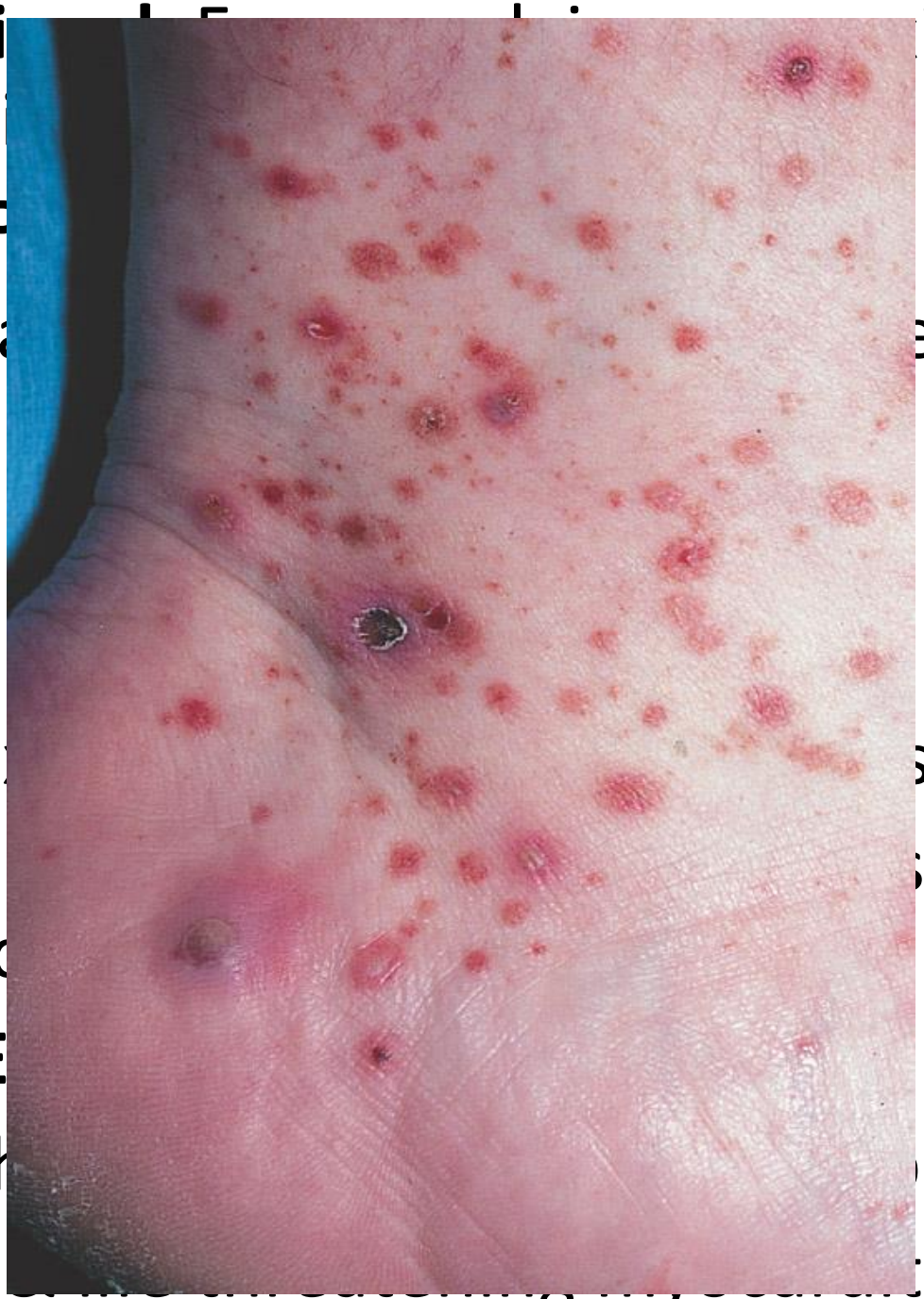
- Proteinuri e (RPGN).
- May be su re

3. **Cutaneou**

- Purpura:
  - Lower e s
  - May be s of ulceratic

4. **Cardiac (E**

- Transient h okinesia
- Infarction is.



5. Respiratory tract (GPA& EGPA):

A. Upper (GPA):

Subglottic stenosis, rhinitis, sinusitis, OM, occular inflammation, septal perforation & saddle nose deformity.

B. Lower:

- Alveolar hge
- Nodular or cavitary lesions (GPA & EGPA)

6. Neurological (EGPA):

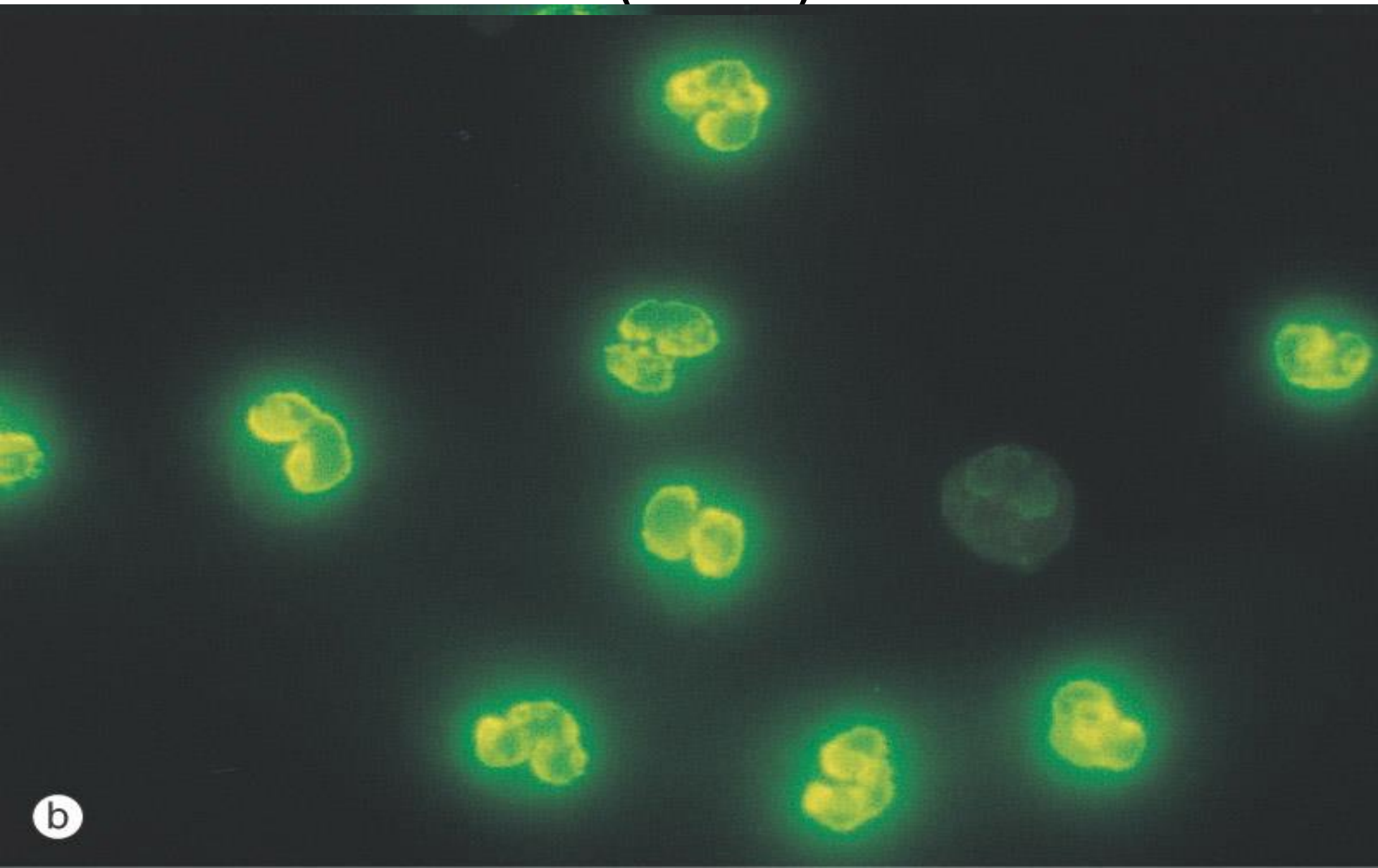
- Peripheral neuropathy: mononeuritis multiplex

7. GIT:

Abdominal pain , blood in stool, mesentric ischemia & rarely intestinal perforation.

Organ System	Frequency of Involvement (%)				
	Microscopic Polyangiitis	*GPA (Wegener)*	*EGPA (Churg-Strauss)*	*IgA Vasculitis (HSP)*	*Cryoglobulinemic Vasculitis*
Kidney	90	80	45	50	55
Skin/cutaneous	40	40	50	90	90
Lungs	50	90	90	<5	<5
Ear, nose, throat	35	90	50	<5	<5
Musculoskeletal	60	60	50	75	70
Neurologic	30	50	60	10	40
Gastrointestinal	50	50	70	60	30

Antineutrophil Cytoplasmic Autoantibodies (ANCA)



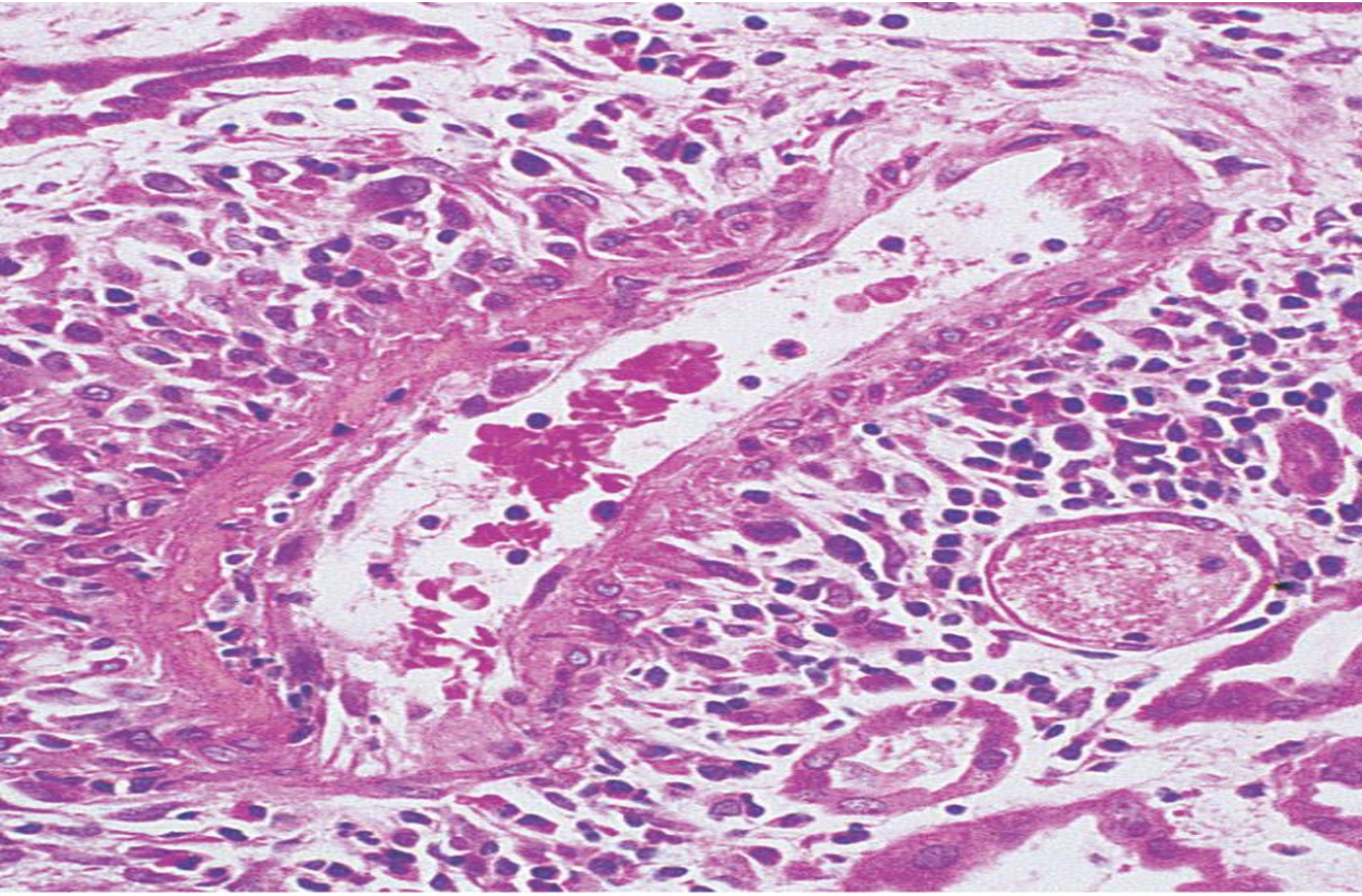
- Good sensitive (80-90%)
- Specificity ?????
- Changes of ANCA titer correlate with disease activity
- 10 – 20% ANCA negative

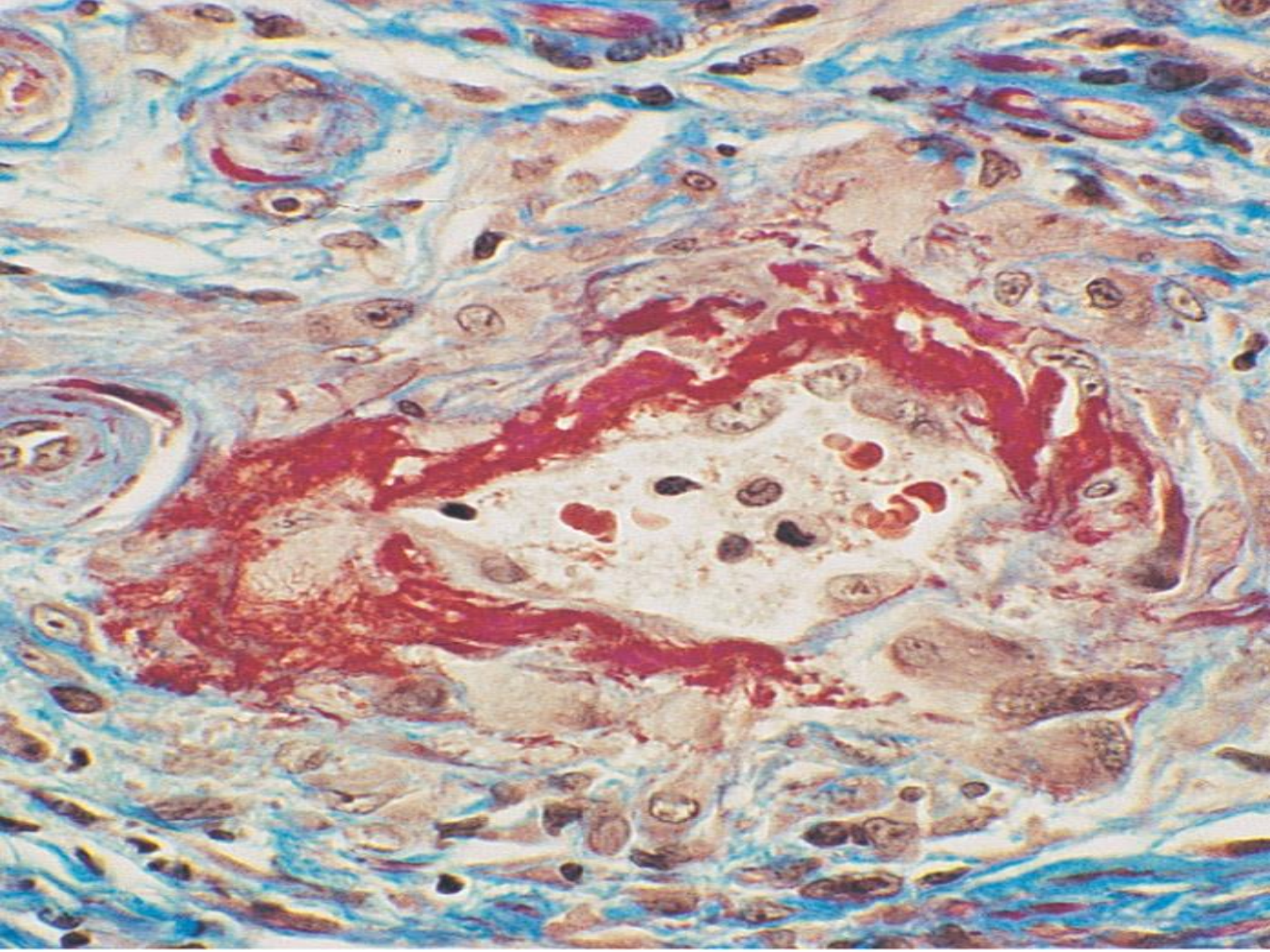
Disorder	Frequency (%)		
	Proteinase 3 (PR3, usually c-ANCA)	*Myeloperoxidase (MPO, usually p-ANCA)*	*Negative*
Granulomatosis with polyangiitis (Wegener)	70	25	5
Microscopic polyangiitis	40	50	10
Eosinophilic granulomatosis with polyangiitis (Churg-Strauss)	5	40	55
Renal-limited pauci-immune crescentic GN	20	70	10

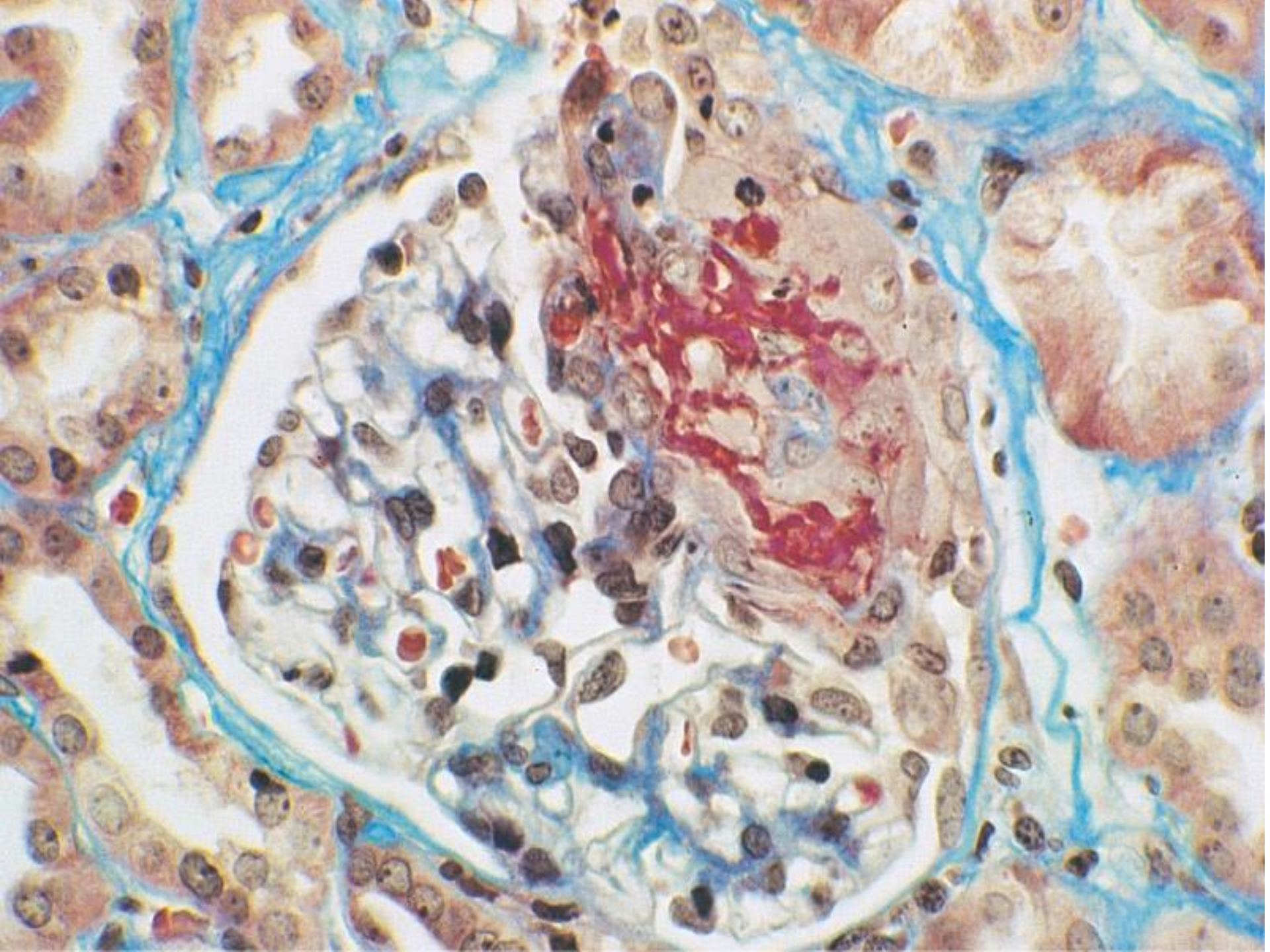
- False positive results:
  - SLE: IFA 25%

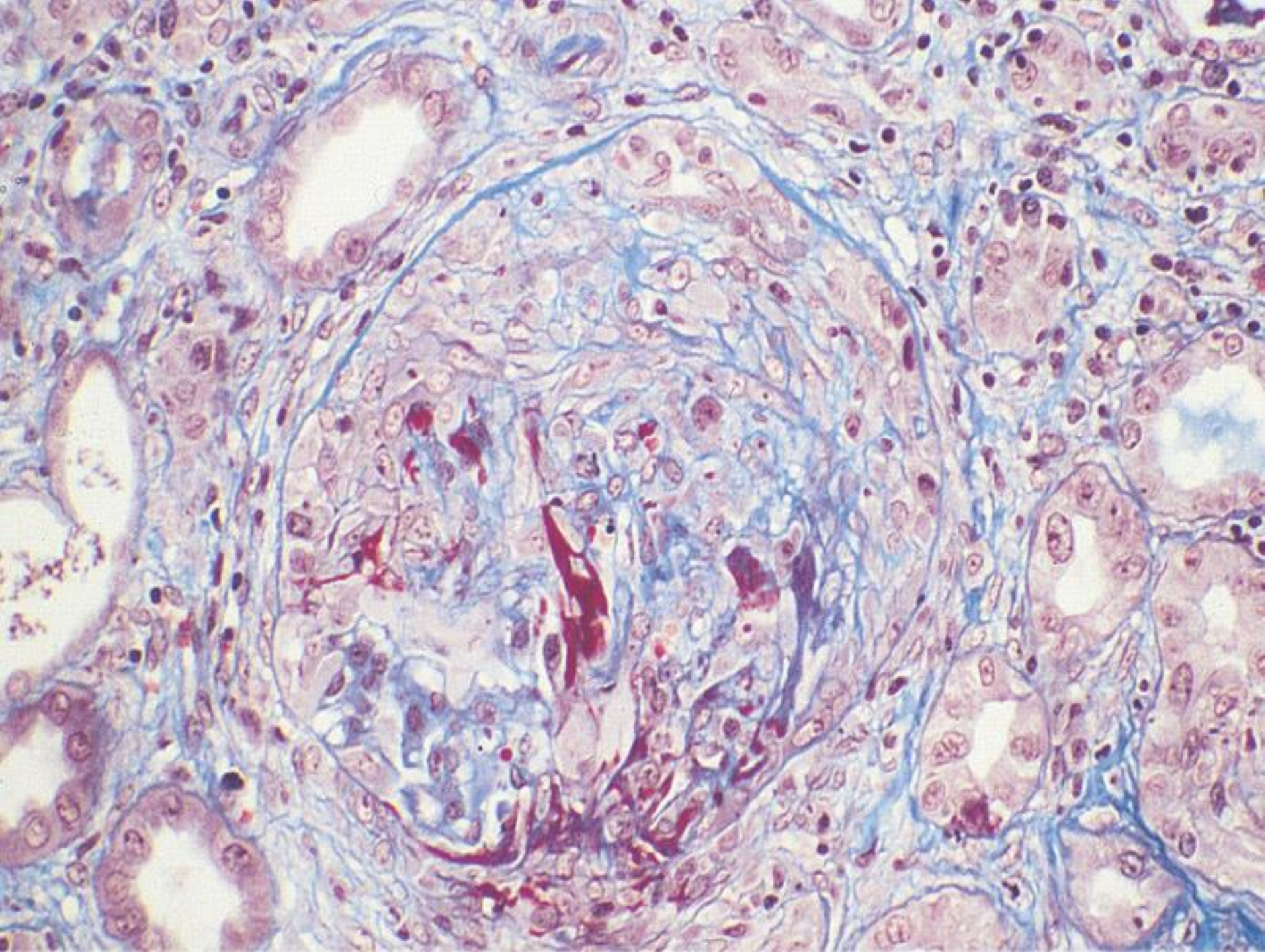
    EIA 5%
  - Anti-GBM disease: 25 – 33%
  - Idiopathic immune complex cescentic GN: 25%
  - IBD
  - Rheumatoid disease
  - Bacterial endocarditis
  - Inflammatory liver disease
  - Cystic fibrosis

Pathology









Histopathological classification

Class	Description	5 year renal survival
Sclerotic	≥50% globally sclerotic glomeruli	50%
Mixed	none of these features predominated	61%
Crescentic	≥50% of glomeruli with cellular crescents	76%
Focal	≥50% normal glomeruli	93%

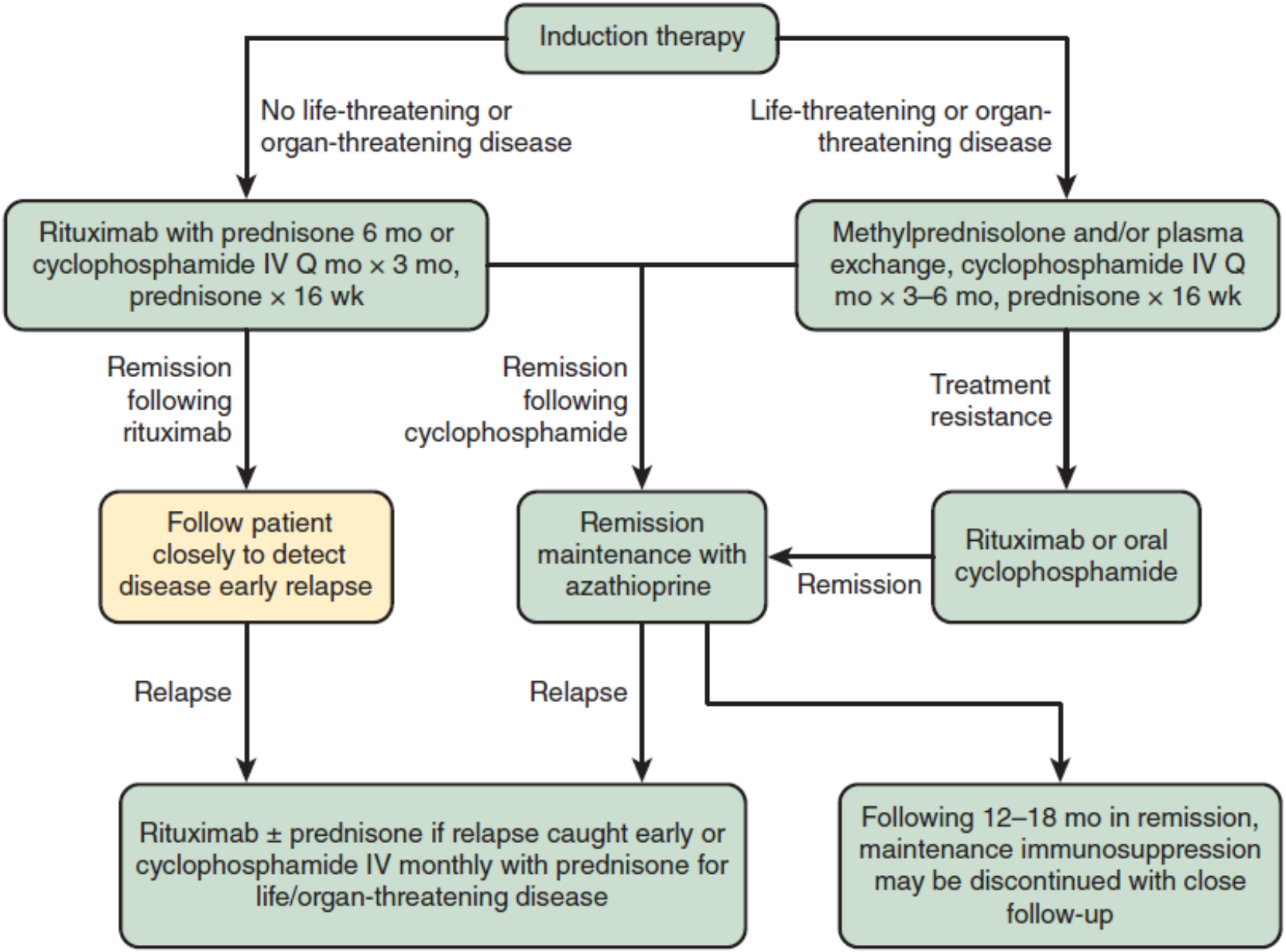
Differential Diagnosis

Features	Microscopic Polyangiitis	GPA (Wegener)	EGPA (Churg-Strauss)	IgA Vasculitis (HSP)	Cryoglobulinemic Vasculitis
Vasculitic signs and symptoms*	+	+	+	+	+
IgA-dominant immune deposits	–	–	–	+	–
Cryoglobulins in blood and vessels	–	–	–	–	+
ANCAs in blood	+	+	+	–	–
Necrotizing granulomas	–	+	+	–	–
Asthma and eosinophilia	–	–	+	–	–

Natural History

- 5-year renal & patient survival: 65 – 75% with adequate immunosupression
- Poor prognostic factors:
  - Older age
  - Pulmonary hge (↑ relapse)
  - Dialysis dependent renal failure
  - PR3 (c-ANCA) (↑ relapse)
  - Advanced glomerulosclerosis, tubular atrophy & interstitial fibrosis

Treatment


Induction therapy
No life-threatening or organ-threatening disease
Life-threatening or organ-threatening disease
Rituximab with prednisone 6 mo or cyclophosphamide IV Q mo × 3 mo, prednisone × 16 wk
Methylprednisolone and/or plasma exchange, cyclophosphamide IV Q mo × 3–6 mo, prednisone × 16 wk
Remission following rituximab
Remission following cyclophosphamide
Treatment resistance
Follow patient closely to detect disease early relapse
Remission maintenance with azathioprine
Remission
Rituximab or oral cyclophosphamide
Relapse
Relapse
Rituximab ± prednisone if relapse caught early or cyclophosphamide IV monthly with prednisone for life/organ-threatening disease
Following 12–18 mo in remission, maintenance immunosuppression may be discontinued with close follow-up

Polyarteritis Nodosa (PAN)

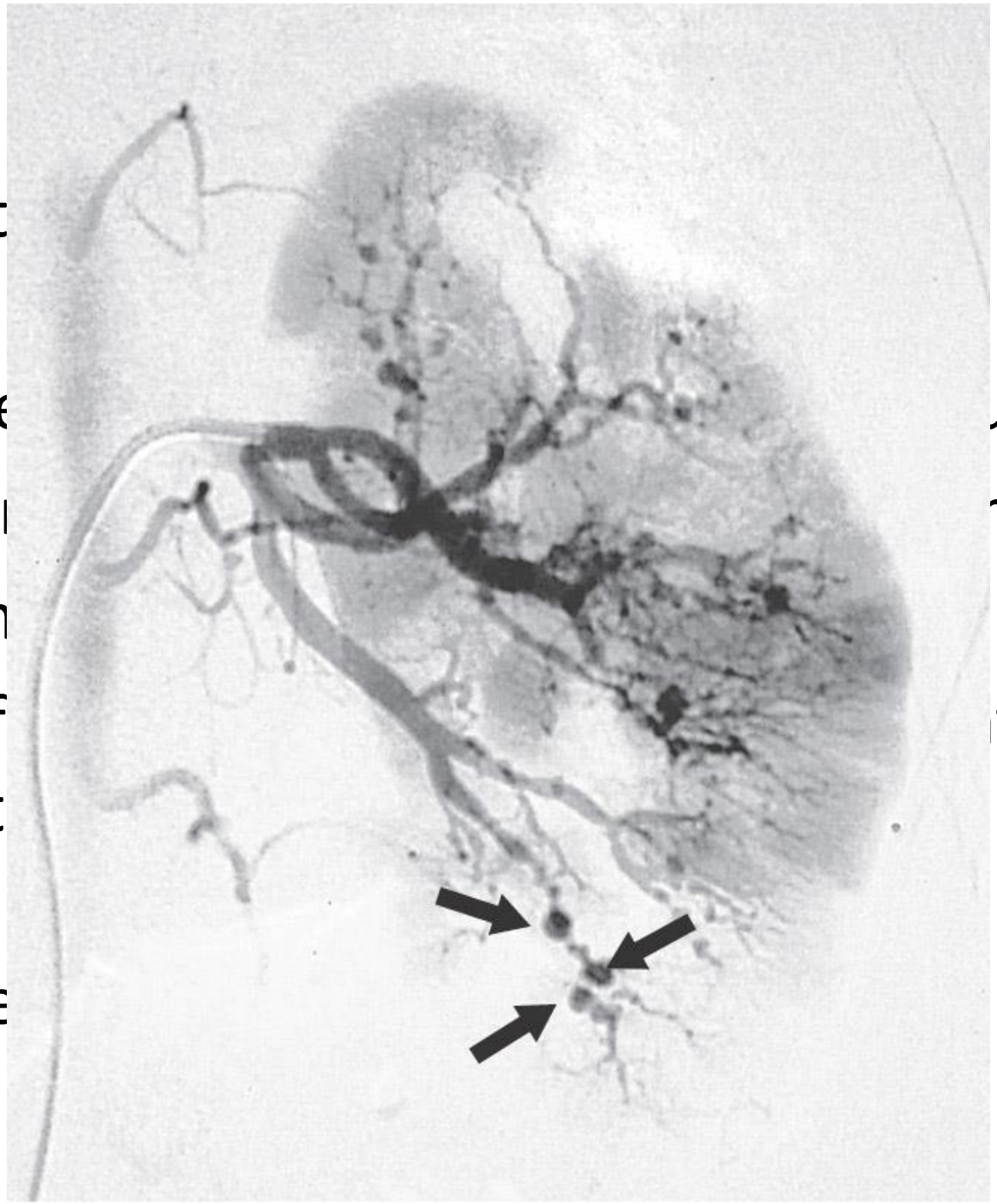
- Definition:

- Systemic necrotizing arteritis affecting main visceral arteries & their intraparenchymal branches
- Only arteritis
- GN excludes diagnosis of PAN
- May be associated with HBV infection

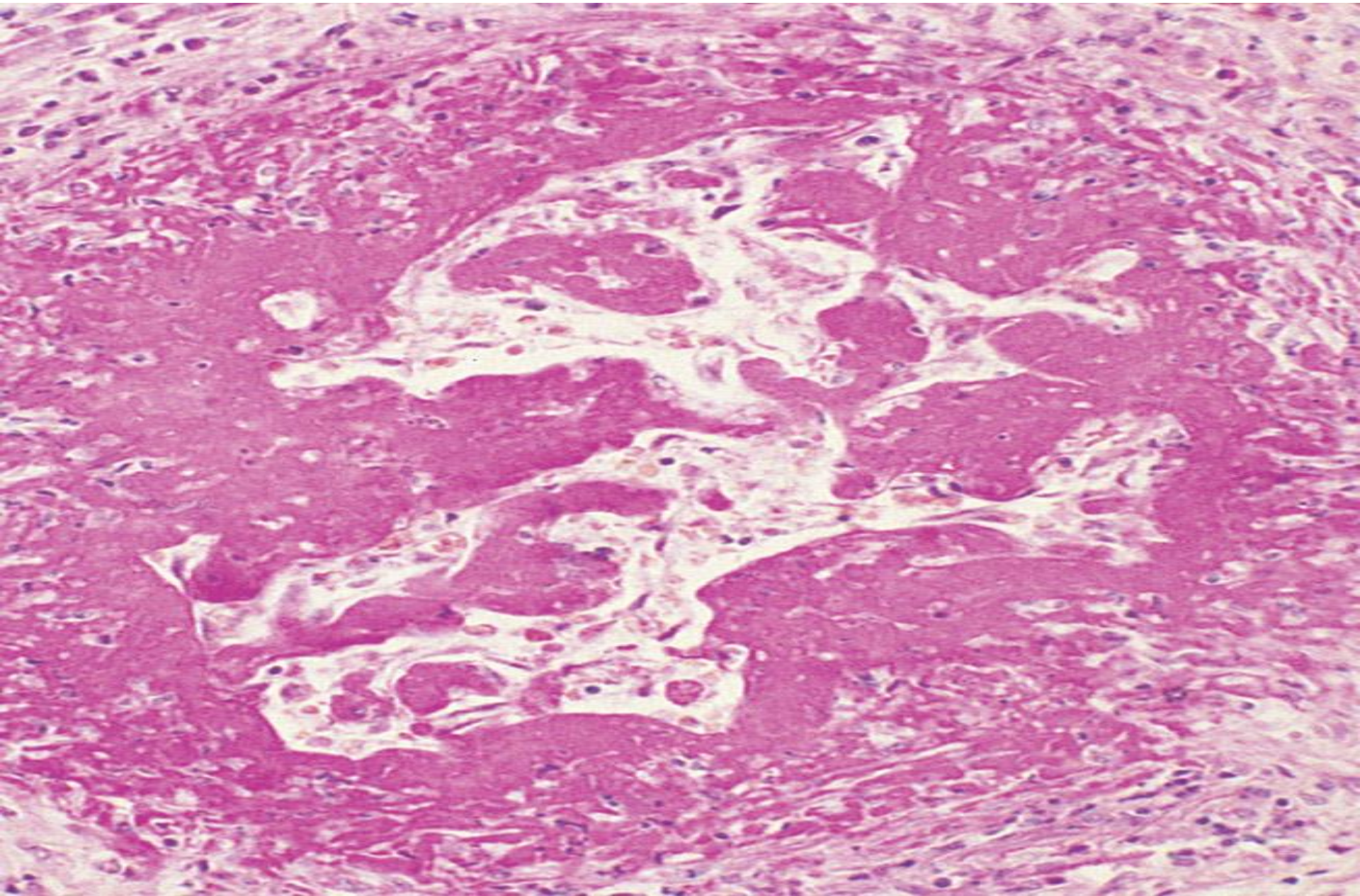
- Epidemiology:

- 3/100,000
- 40 – 60 years
- Male = Female

1. Constit & weight loss
2. Periphe ltiplex
3. Renal i naturia
4. Abdom
5. Red inf farction, ulcerat
6. Arteria not comple



Pathology



Differential Diagnosis

Polyarteritis Nodosa and Microscopic Polyangiitis: Distinguishing Features		
Clinical Feature	**Polyarteritis Nodosa**	**Microscopic Polyangiitis**
Microaneurysms by angiography	Yes	No (rare)
Rapidly progressive nephritis	No	Yes (very common)
Pulmonary hemorrhage	No	Yes
Renovascular hypertension	Yes (10%-33%)	No
Peripheral neuropathy	Yes (50%-80%)	Yes (10%-20%)
Positive hepatitis B serology	Uncommon	No
Positive ANCA	Rare	Frequent
Relapses	Rare	Frequent

Natural History

- 10- year survival: 80% with appropriate ttt
- 15% with remission develop relapse
- Poor prognostic factors:
  - Age > 50 years
  - Cardiac involvement
  - Gut involvement
  - Renal involvement

Treatment

- No risk factors for poor outcome: Steroids only
- With risk factors for poor outcome: Steroids + cytotoxic drugs (cyclophosphamide)
- With HBV infection (EULAR recommendations):
  - Initial ttt with high dose steroids tapered during 2 weeks
  - followed by antiviral therpay
  - ± Plasma exchange

Kawasaki Disease

- Definition:

- Acute febrile illness
- Usually in young children (< 1 year)
- With MCLN syndrome
- Clinically significant renal affection is very rare

- Epidemiology:

- First described in Japan
- Occur worldwide
- Japan: 50/100,000 children < 5 years

Clinical features

1. Arteritis:
   - Most often manifest as cardiac disease
   - Most common cause of childhood MI

2. MCLN syndrome:
   - Fever (38 – 40)
   - Mucosal inflammation
   - Swollen red tongue (Strawberry tongue)
   - Polymorphous erythematous rash
   - Indurative edema of the extremeties
   - Erythema of palms & soles
   - Conjunctival injection
   - Enlarged LN

Natural history

- Self limited with ttt by IVIG
- 1% develop severe coronary complications

Treatment

- Aspirin + IVIG
- Steroids may increase coronary complications

Takayasu Arteritis & Giant Cell Arteritis

- Definition:

- Affect aorta & its major branches
- GCA affects commonly extracranial branches of carotid artery
- GCA is associated with polymyalgia rheumatica
- TA affects commonly major arteries supplying the extremeties

- Epidmiology:

- GCA: Female : Male = 4:1 >50 years
- TA: Female : Male = 9:1 10 – 20 years

Clinical features

A. Takayasu arteritis:

- Reduced peripheral pulse
- Vascular bruit
- Claudication
- Renovascular HTN

B. Giant cell arteritis:

- Headache (most common)
- Temporal artery tenderness, nodularity & reduced pulses (50%)
- Blindness, deafness, jaw claudication, tongue dysfunction.
- Polymyalgia rheumatica (> 50%): stiffness & aching in neck & proximal muscles of the shoulders & hips

Treatment

- Corticosteroids
- Cytotoxic drugs in resistant diseases
- Low dose aspirin in GCA
- Renovascular HTN (TA):
  - Medical therapy
  - Reconstructive bypass surgery or angioplasty during quiescent phase of the disease

Vasculitis Categories and Definitions

Category/Name	Definition
Large-Vessel Vasculitis	
Takayasu arteritis	Arteritis, often granulomatous, predominantly affecting aorta and/or its major branches. Onset usually in patients younger than 50.
Giant cell arteritis	Arteritis, often granulomatous, usually affecting aorta and/or its major branches, with predilection for branches of carotid and vertebral arteries; often involves temporal artery. Onset usually in patients older than 50 and often associated with polymyalgia rheumatica.
Medium-Vessel Vasculitis	
Polyarteritis nodosa	Necrotizing arteritis of medium or small arteries without glomerulonephritis (GN) or vasculitis in arterioles, capillaries, or venules; and not associated with ANCA.
Kawasaki disease	Arteritis associated with mucocutaneous lymph node syndrome and predominantly affecting medium and small arteries; coronary arteries are often involved; aorta and large arteries may be involved. Usually occurs in infants and young children.
Small-Vessel Vasculitis	
ANCA-Associated Small-Vessel Vasculitis	
	Necrotizing vasculitis, with few or no immune deposits, predominantly affecting small vessels (capillaries, venules, arterioles, small arteries), associated with MPO-ANCA or PR3-ANCA. Not all patients have ANCA. Add prefix indicating ANCA reactivity, e.g., PR3-ANCA, MPO-ANCA, ANCA-negative.
Microscopic polyangiitis (MPA)	Necrotizing vasculitis, with few or no immune deposits, predominantly affecting small vessels (capillaries, venules, arterioles). Necrotizing arteritis involving small and medium arteries may be present. Necrotizing GN is common. Pulmonary capillaritis often occurs. Granulomatous inflammation is absent.
Granulomatosis with polyangiitis (Wegener) (GPA)	Necrotizing granulomatous inflammation usually involving upper and lower respiratory tract, and necrotizing vasculitis affecting predominantly small to medium vessels (capillaries, venules, arterioles, arteries, veins). Necrotizing GN is common.
Eosinophilic granulomatosis with polyangiitis (Churg-Strauss) (EGPA)	Eosinophil-rich and necrotizing granulomatous inflammation often involving the respiratory tract, and necrotizing vasculitis predominantly affecting small to medium vessels, and associated with asthma and eosinophilia. ANCA is more common when GN is present.
Immune Complex Small-Vessel Vasculitis	
	Vasculitis with moderate to marked vessel wall deposits of immunoglobulin and/or complement components predominantly affecting small vessels (capillaries, venules, arterioles, small arteries). GN is common.
Anti–glomerular basement membrane (anti-GBM) disease	Vasculitis affecting glomerular capillaries, pulmonary capillaries, or both, with basement membrane deposition of anti–basement membrane autoantibodies. Lung involvement causes pulmonary hemorrhage, and renal involvement causes GN with necrosis and crescents.
Cryoglobulinemic vasculitis	Vasculitis with cryoglobulin immune deposits affecting small vessels (predominantly capillaries, venules, or arterioles) and associated with cryoglobulins in serum. Skin, glomeruli, and peripheral nerves are often involved.
IgA vasculitis (IgAV) (Henoch-Schönlein purpura)	Vasculitis, with IgA1-dominant immune deposits, affecting small vessels (predominantly capillaries, venules, or arterioles). Often involves skin and gastrointestinal tract and frequently causes arthritis. GN indistinguishable from IgA nephropathy may occur.
Hypocomplementemic urticarial vasculitis (anti-C1q vasculitis)	Vasculitis accompanied by urticaria and hypocomplementemia affecting small vessels (capillaries, venules, arterioles), and associated with anti-C1q antibodies. GN, arthritis, obstructive pulmonary disease, and ocular inflammation are common.

Thank You