Vasculitis

CVS 7

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Lecture 7

- Vasculitis – pathology of polyarteritis nodosa, giant cell arteritis and Buerger's disease. ANCA mediated vasculitis (Wegener's granulomatosis and hypersensitivity/ leukocytoclastic vasculitis)

Vasculitis

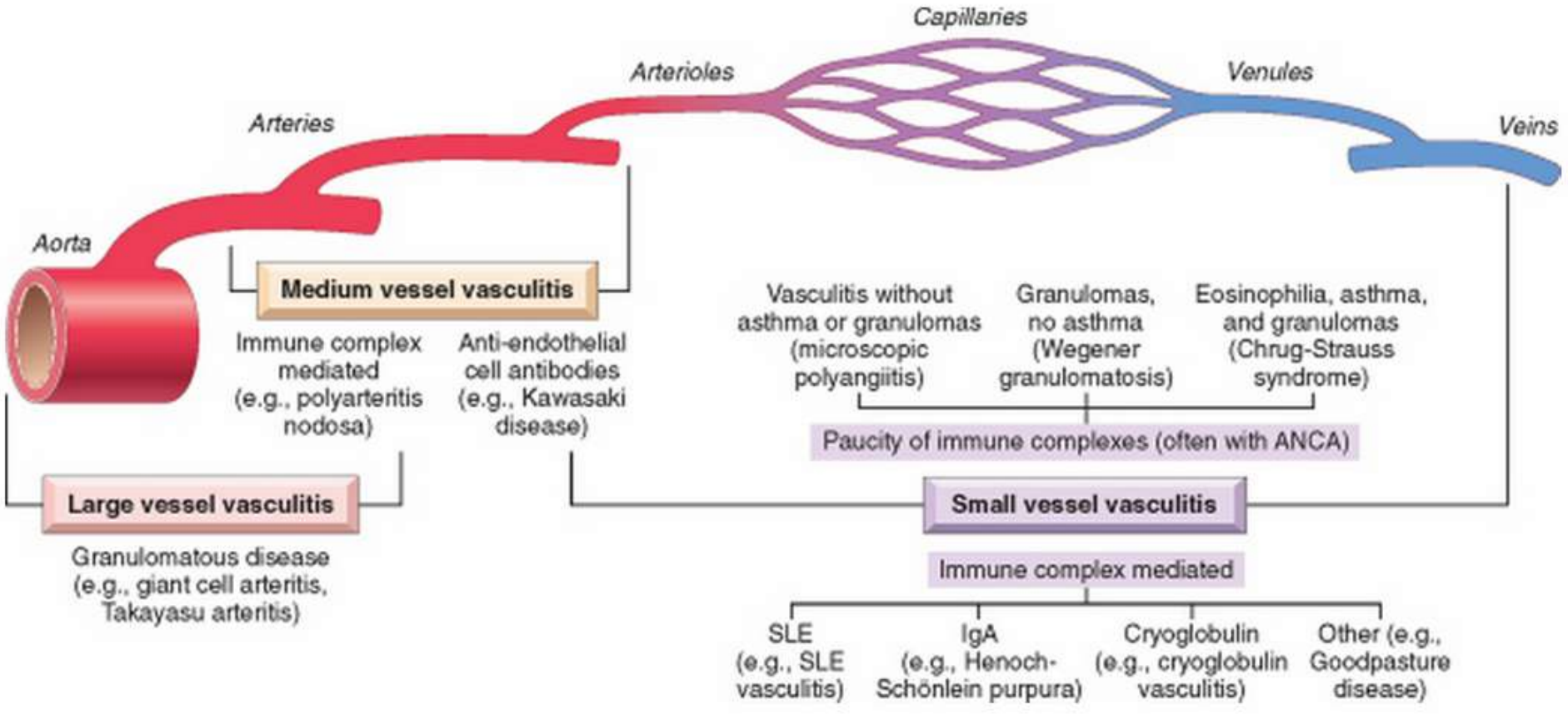
Vascular inflammatory injury, often with necrosis

Vasculitis

Causes

- immune-mediated :
  - Immune complex deposition
  - Antineutrophil cytoplasmic antibodies (ANCAs)
  - Anti-endothelial cell antibodies

- invasion of vascular walls by infectious pathogens
- Physical and chemical injury

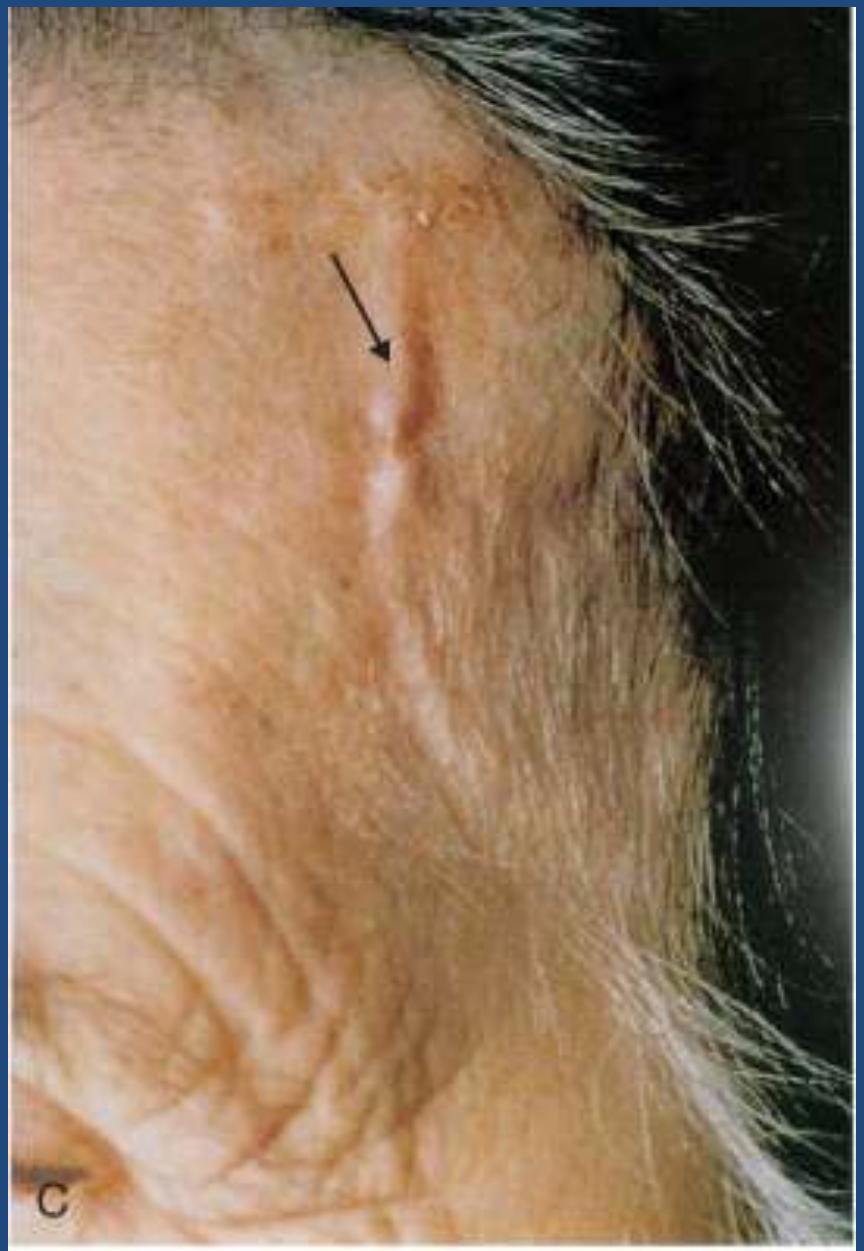

Capillaries
Arterioles
Venules
Arteries
Veins
Aorta
Medium vessel vasculitis
Immune complex mediated (e.g., polyarteritis nodosa)
Anti-endothelial cell antibodies (e.g., Kawasaki disease)
Vasculitis without asthma or granulomas (microscopic polyangiitis)
Granulomas, no asthma (Wegener granulomatosis)
Eosinophilia, asthma, and granulomas (Chrug-Strauss syndrome)
Paucity of immune complexes (often with ANCA)
Large vessel vasculitis
Granulomatous disease (e.g., giant cell arteritis, Takayasu arteritis)
Small vessel vasculitis
Immune complex mediated
SLE (e.g., SLE vasculitis)
IgA (e.g., Henoch-Schönlein purpura)
Cryoglobulin (e.g., cryoglobulin vasculitis)
Other (e.g., Goodpasture disease)

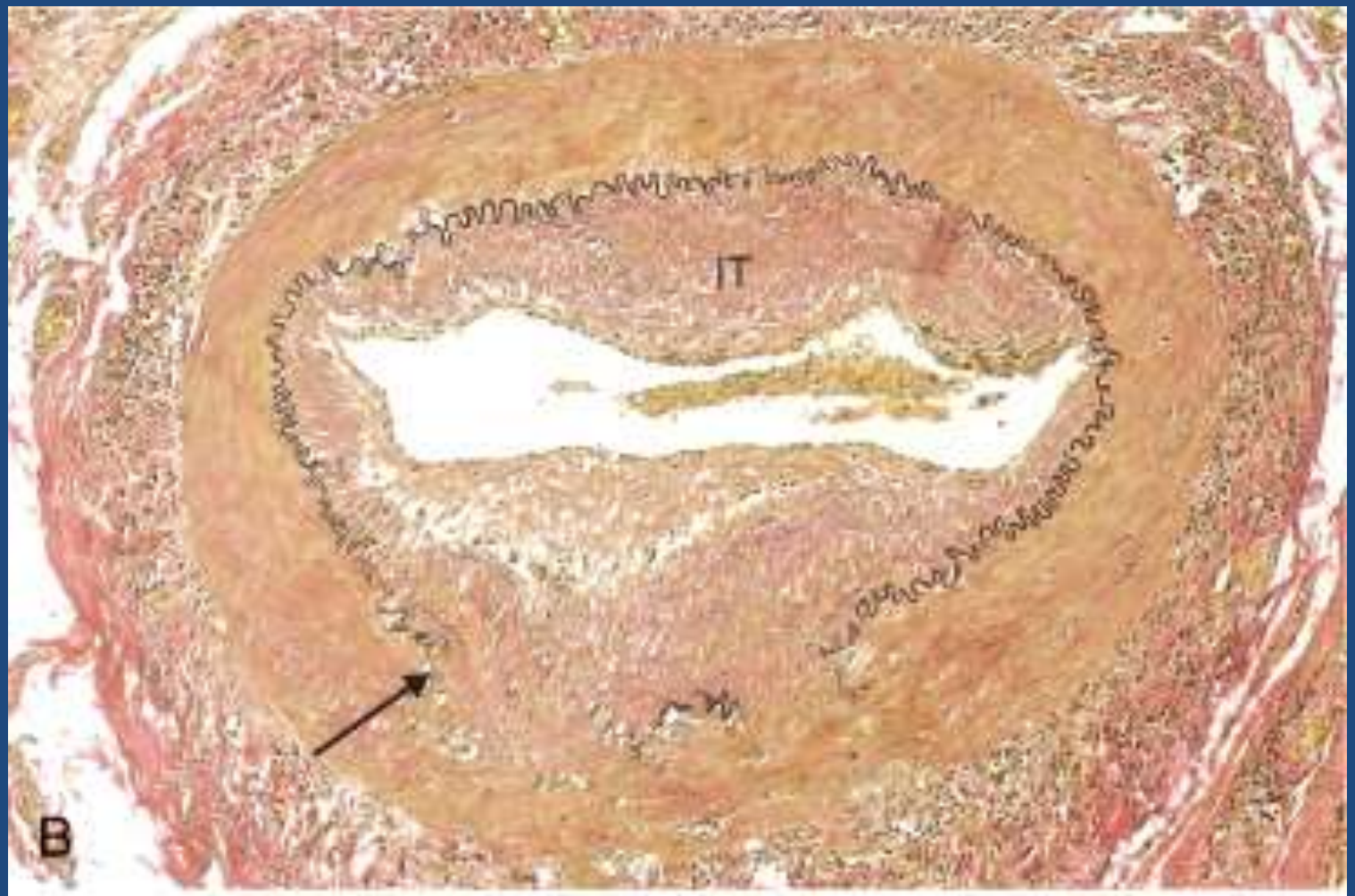
Giant-Cell (Temporal) Arteritis

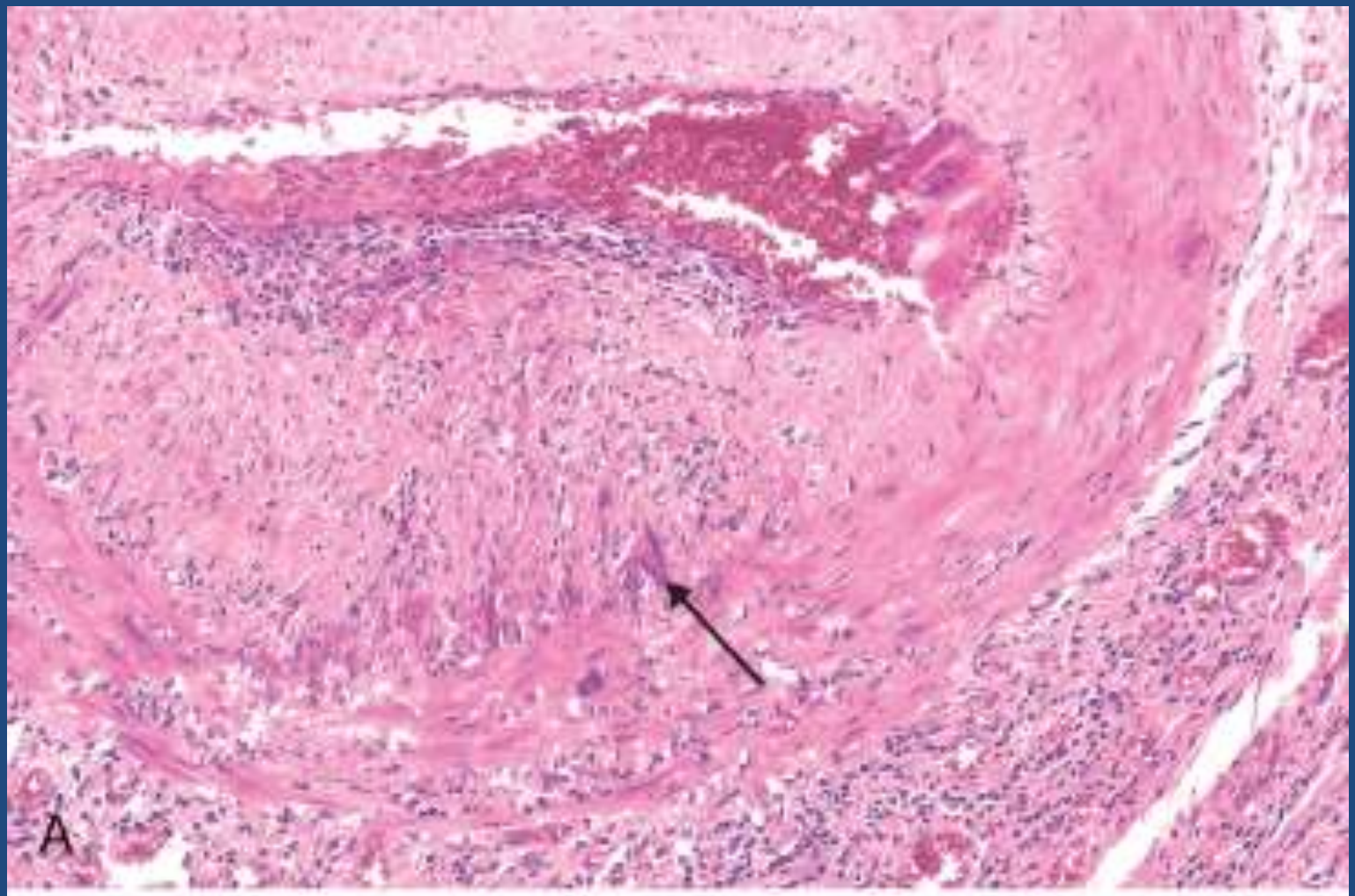
- The most common
- Chronic, typically granulomatous inflammation of large to small-sized arteries
- Principally affects the arteries in the head- especially the temporal arteries
- Rarely the aorta (*giant-cell aortitis*)

Giant-Cell (Temporal) Arteritis

- Unknown cause
- Likely immune origin, T cell-mediated







Giant-Cell (Temporal) Arteritis
Clinical features

- > 50 years of age
- Vague symptoms:
  - Fever, fatigue and weight loss
- May involve facial pain or headache
- Most intense along the course of the superficial temporal artery, which is painful to palpation

Giant-Cell (Temporal) Arteritis

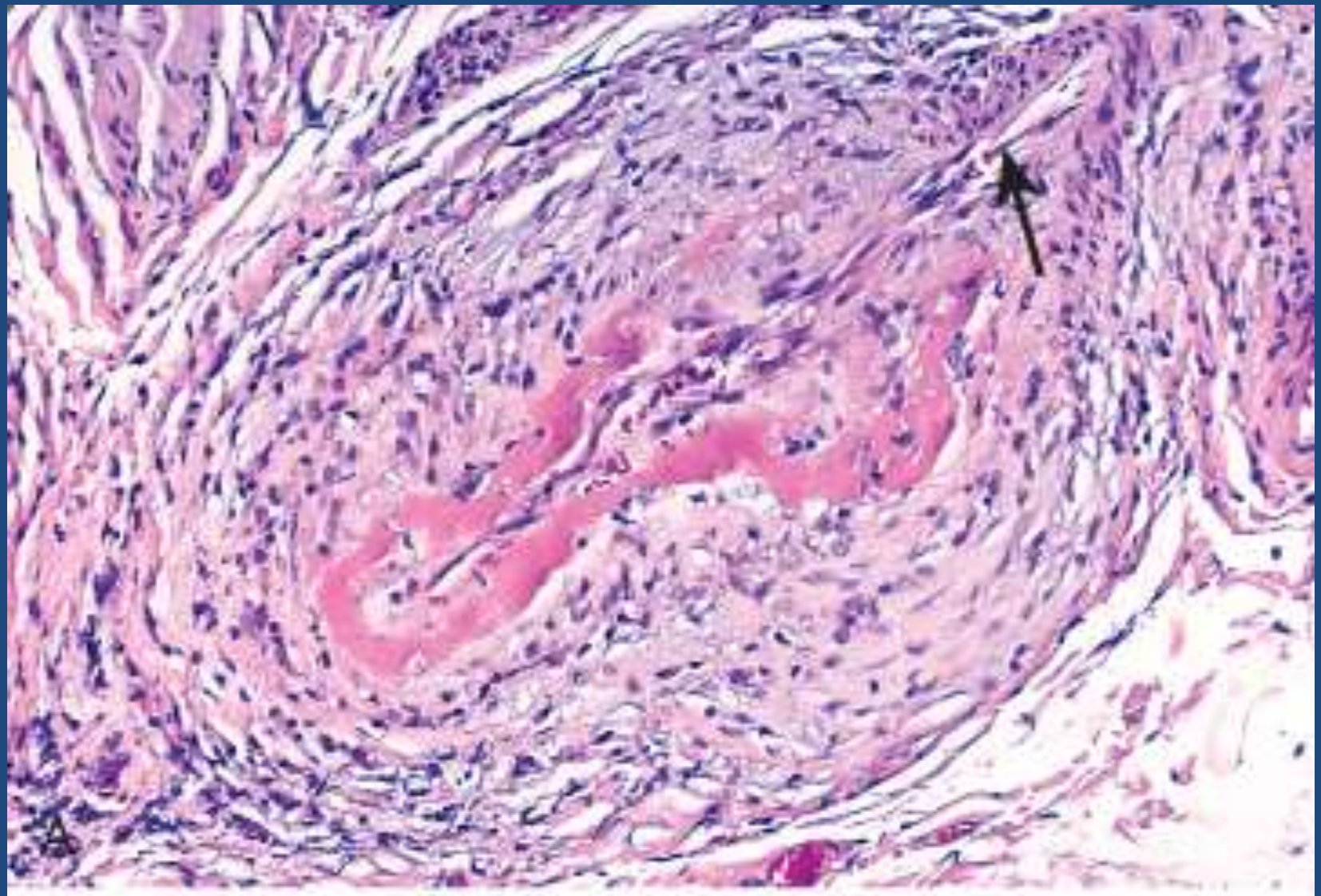
- Definite diagnosis depends on:

biopsy of an adequate segment and histological confirmation

- Treatment: corticosteroids

Polyarteritis Nodosa

- Systemic
- Small or medium-sized muscular arteries
- But **not** arterioles, capillaries, or venules
- Typically involving renal and visceral vessels but **sparing** the pulmonary circulation

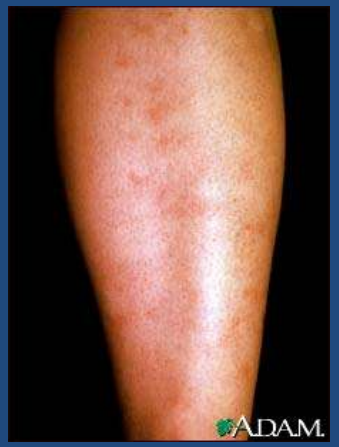


Polyarteritis Nodosa

- all stages of activity (from early to late) may coexist in different vessels or even within the same vessel

Polyarteritis Nodosa
Clinical picture

- Largely young adults
- Typically episodic, with long symptom-free intervals
- Because the vascular involvement is widely scattered, the clinical findings may be varied and puzzling



Polyarteritis Nodosa
Clinical picture

- Fever and weight loss
- Examples on systemic involvement:
  - Renal (arterial) involvement is common and a major cause of death
  - Hypertension, usually developing rapidly
  - Abdominal pain and melena (bloody stool)
  - Diffuse muscular aches and pains
  - Peripheral neuritis
- Biopsy is often necessary to confirm the diagnosis

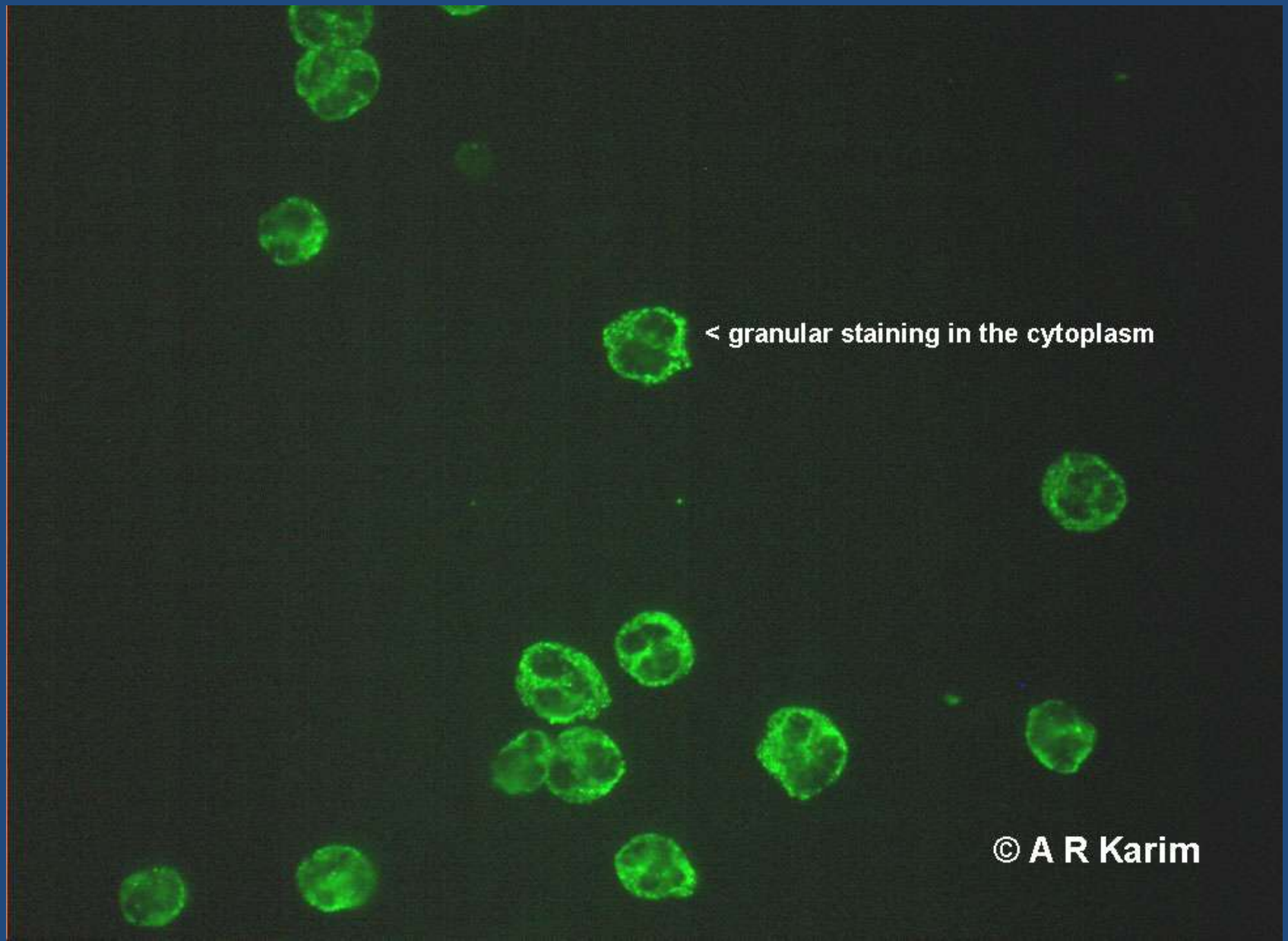
Polyarteritis Nodosa

- **No** association with ANCA
- Some 30% of patients with PAN have hepatitis B antigenemia
- If untreated, the disease is fatal in most cases
- Therapy with corticosteroids and other immunosuppressive therapy results in remissions or cures in 90%

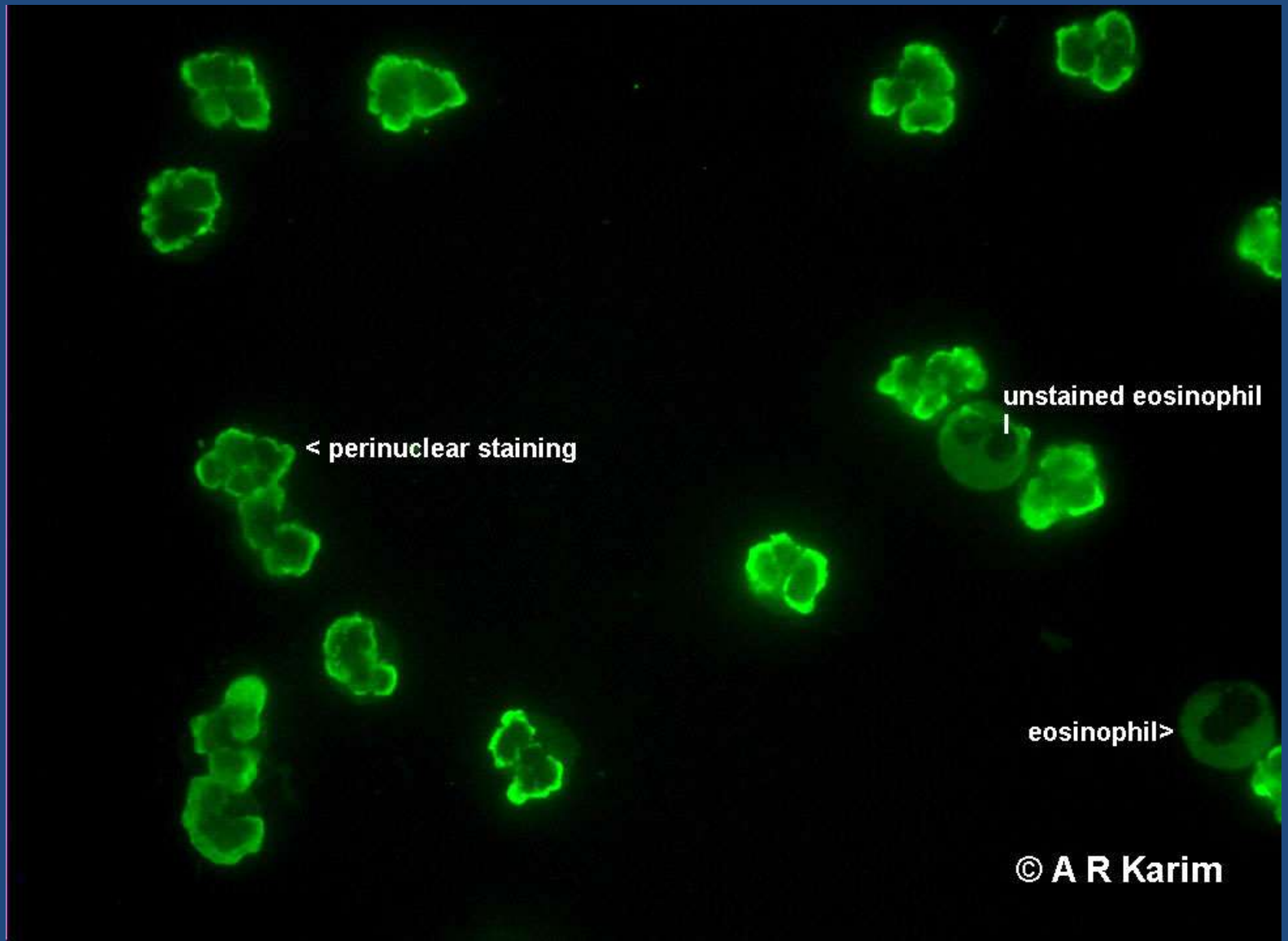
Polyarteritis Nodosa
Complications

- Vessel rupture
- Impaired perfusion:
  - Ulcerations
  - Infarcts
  - Ischemic atrophy *(not infarction)*
  - Haemorrhages in the distribution of affected vessels may be the first sign of disease

c-ANCA



p-ANCA


unstained eosinophil
l
< perinuclear staining
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Antineutrophil Cytoplasmic Antibodies

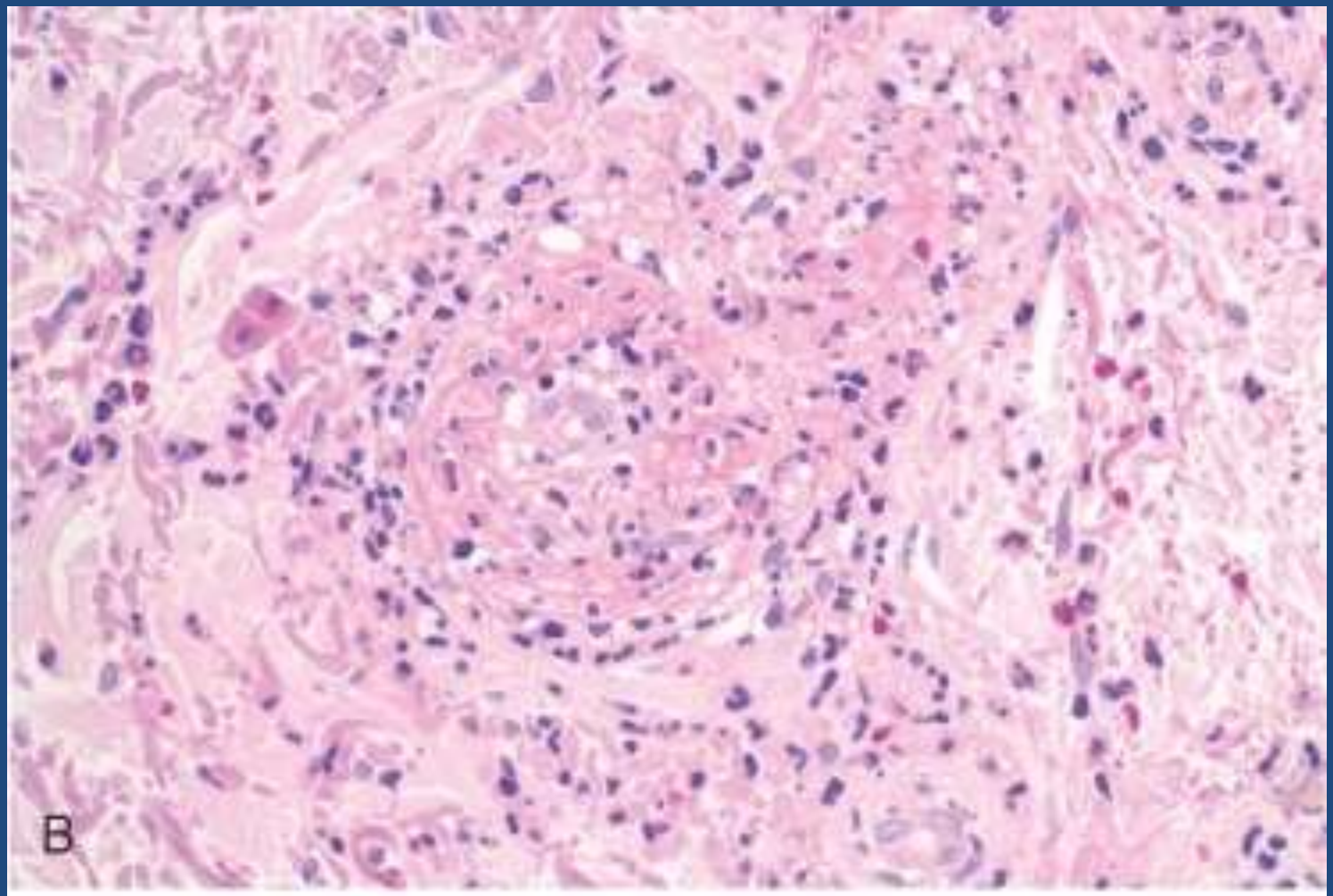
- Cytoplasmic localization (c-ANCA) -> the most common target antigen is proteinase-3 (PR3)
  - typical of Wegener granulomatosis
- Perinuclear localization (p-ANCA) -> most of the autoantibodies are specific for myeloperoxidase (MPO)
  - microscopic polyangiitis and Churg-Strauss syndrome
- ANCAs serve as useful diagnostic markers for the ANCA-associated vasculitides
- Their levels can reflect the degree of inflammatory activity

Microscopic Polyangiitis

- Necrotizing vasculitis that generally affects capillaries as well as arterioles and venules of a size smaller than those involved in PAN
- Rarely, larger arteries may be involved
- *All lesions of microscopic polyangiitis tend to be of the same age in any given patient*
- *Necrotizing glomerulonephritis (90% of patients) and pulmonary capillaritis are particularly common*

Microscopic Polyangiitis
Pathogenesis

- In many cases, an antibody response to antigens such as drugs (e.g., penicillin), microorganisms (e.g., streptococci), heterologous proteins, or tumor proteins is the presumed cause
- This can result in immune complex deposition, or it may trigger secondary immune responses
- p-ANCAs are present in more than 70% of patients

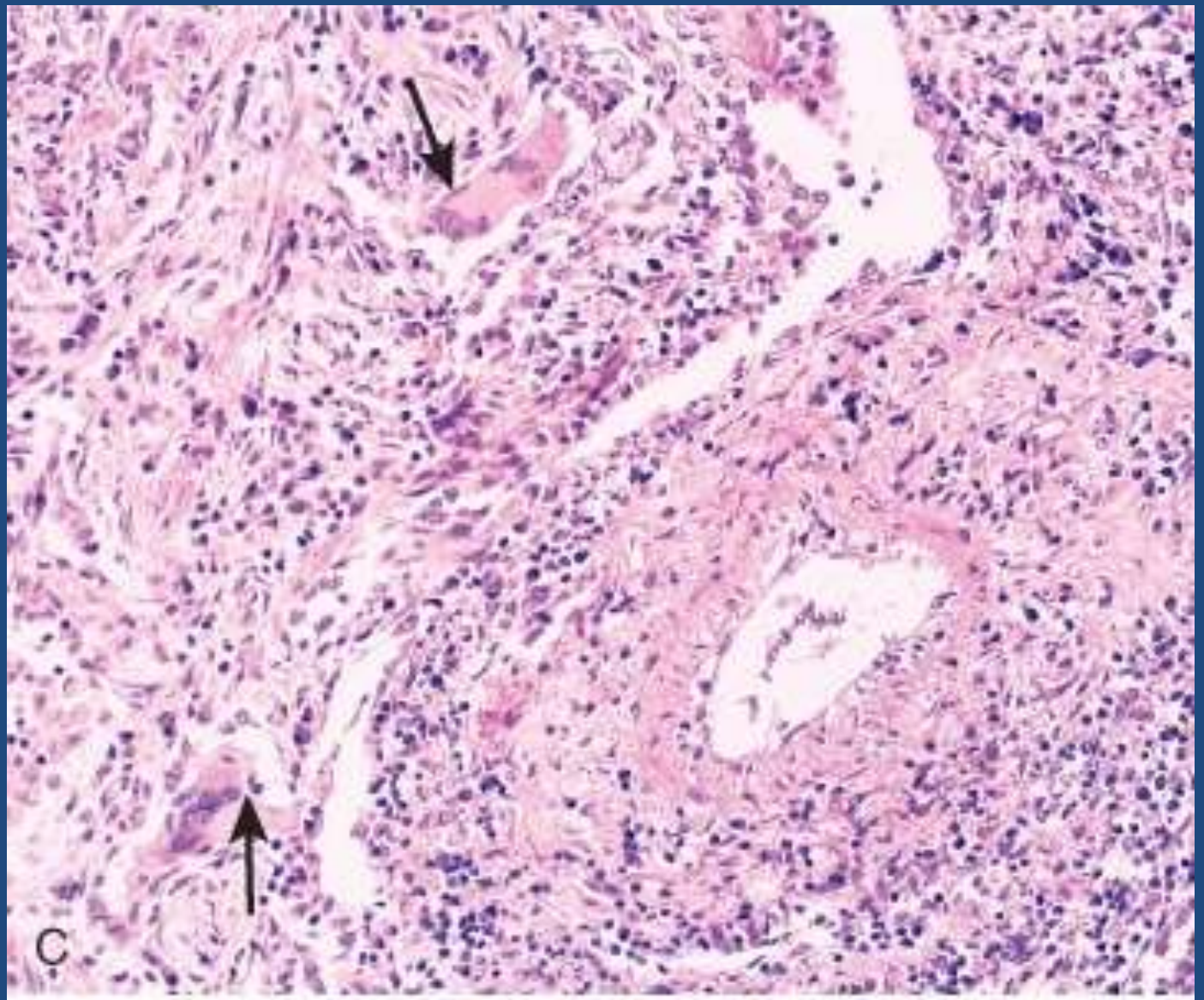


Microscopic Polyangiitis

- Depending on the organ involved, major clinical features include:
  - Hemoptysis
  - Hematuria and proteinuria
  - Bowel pain or bleeding
  - Muscle pain or weakness
  - Palpable cutaneous purpura

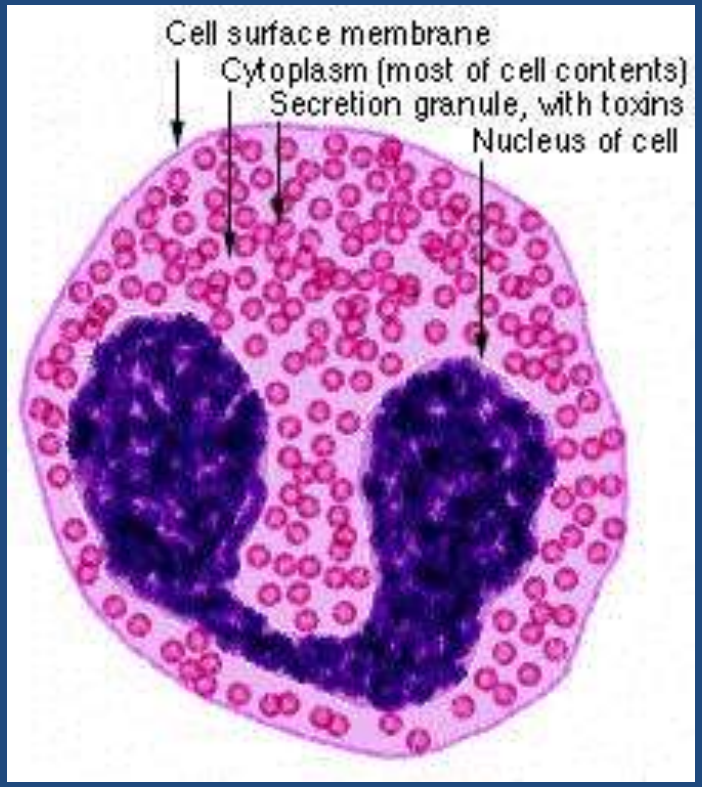
Wegener Granulomatosis

- Triad:
  - *Acute necrotizing granulomas* of the upper and lower respiratory tract (lung), or both
  - *Necrotizing or granulomatous vasculitis* affecting small to medium-sized vessels (most prominent in the lungs and upper airways)
  - *Focal necrotizing, often crescentic, glomerulitis*



Wegener Granulomatosis

- 40-50 years
- Without Rx -> 80% die
- With Rx -> 90% live (not cured)
- The Rx -> immunosuppression


Cell surface membrane
Cytoplasm (most of cell contents)
Secretion granule, with toxins
Nucleus of cell

Churg-Strauss syndrome

- Eosinophil-rich and granulomatous inflammation involving the respiratory tract and necrotizing vasculitis affecting small vessels
- Associated with asthma and blood eosinophilia
- Associated with p-ANCAs.

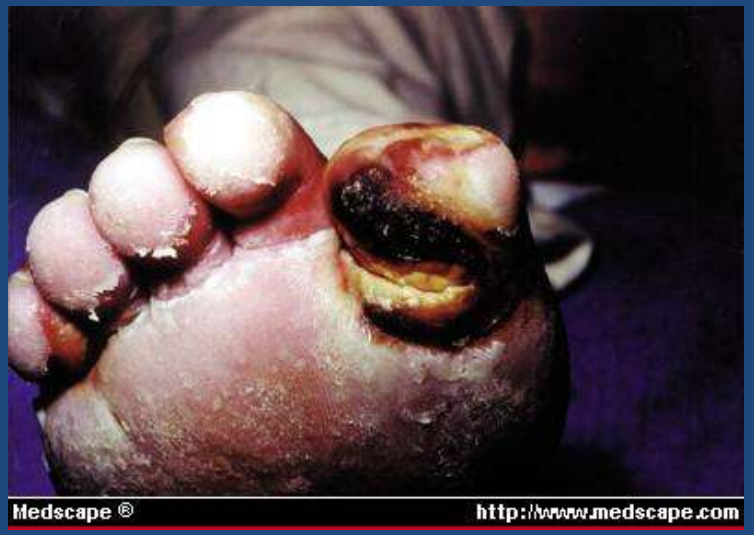
Churg-Strauss syndrome

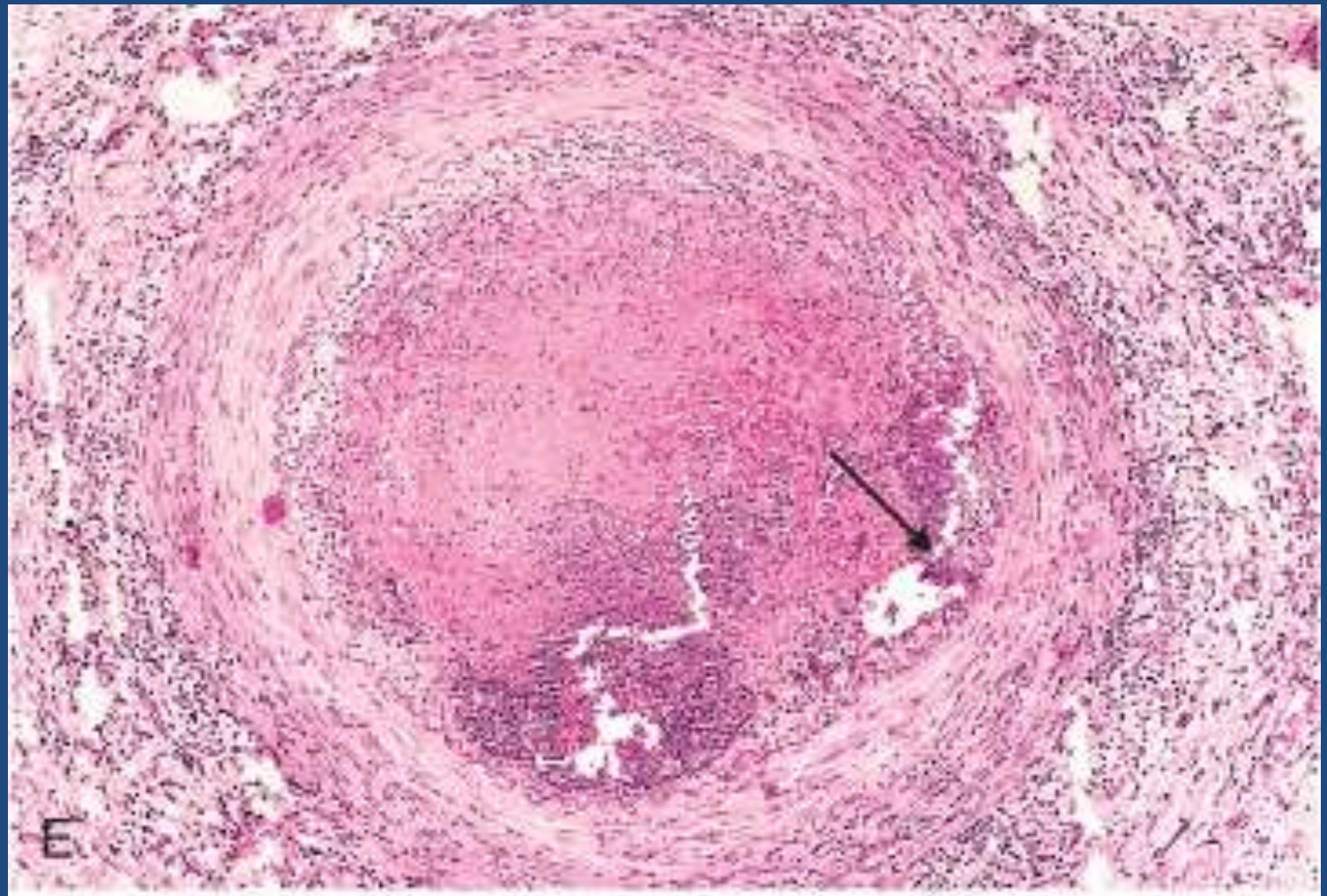
- strong association with
  - Allergic rhinitis
  - Bronchial asthma
  - Eosinophilia
- Vessels in the lung, heart, spleen … are frequently involved by:
  - intravascular and extravascular granulomas
  - infiltration of vessels and perivascular tissues by eosinophils is striking

Thromboangiitis obliterans (Buerger disease)

Thromboangiitis obliterans (Buerger disease)

- Segmental, thrombosing acute and chronic inflammation of medium-sized and small arteries
- Tibial and radial arteries, with occasional secondary extension into extremity veins and nerves
- Unknown cause





Thromboangiitis obliterans
Clinical picture

- Heavy smoker
- Begins before the age of 35 years
  - Superficial nodular phlebitis
  - Cold sensitivity of the Raynaud type in the hands (see figure below)
  - Pain in the instep of the foot induced by exercise (so-called *instep claudication*)

Thromboangiitis obliterans

- In contrast to the vascular insufficiency caused by atherosclerosis, in Buerger disease the insufficiency tends to be accompanied by **severe pain,** even at rest, related undoubtedly to the neural involvement
- Chronic ulcerations of the toes, feet, or fingers may appear, perhaps followed in time by frank gangrene
- Abstinence from cigarette smoking in the early stages of the disease often brings dramatic relief from further attacks