Vasculitis

Associated w/ scattered Nodules
وتحتم
Ischemia

Hypertension:-
According to the New Guidelines:-
هيك سؤال إلباشو اذا بدها تسأل عن قيم Blood Pressure

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- Inflammation of the walls of vessels is called *vasculitis*

→ may lead to any type to clinical disease!

- It is encountered in diverse clinical settings.

- Vessels of any type in virtually any organ can be affected.

Clinical manifestations often include:

1. constitutional signs & symptoms: e.g., fever, myalgias, arthralgias, & malaise.
2. local manifestations of downstream tissue ischemia.

⊕ Generalized Fatigue + Disease

Several vasculitides tend to affect only vessels of a particular size or location, but Most vasculitides affect small vessels; from arterioles to capillaries to venules

- 20 primary forms of vasculitis → classification schemes → according to: vessel diameter, role of immune complexes, presence of specific autoantibodies, granuloma formation, organ specificity, & even population demographics
- The two most common mechanisms of vasculitis are:
  - direct invasion of vascular walls by infectious pathogens
  - Immune-mediated mechanisms .
- Physical & chemical injury, such as irradiation, mechanical trauma, & toxins can also cause vascular damage.

Pathogenesis of Noninfectious Vasculitis

Immunologic injury in noninfectious vasculitis may be caused by:

(1) **Immune complex deposition**

(2) **Antineutrophil cytoplasmic antibodies (ANCA)**

(3) **Anti-endothelial cell antibodies. (Anti-EC)**

→ Diagnosed by blood-sample

(4) **Autoreactive T cells**

Non infectious:-

Immune Complex–Associated Vasculitis

- ✓ This mechanism is supported by the fact that the vascular lesions resemble those found in experimental immune complex - mediated conditions. (in situ / circulation)
- ✓ Also in some cases contain readily identifiable antibody and complement.
- ✓ is a diagnostic challenge; rarely is the specific antigen responsible for immune complex formation known, & in most instances it is not clear whether the pathogenic antigen-antibody complexes are deposited into the vessel wall from the circulation or form in situ.

- **Systemic lupus erythematosus & polyarteritis nodosa**
  - ↑ females
  - Arthritis, Neuropathy, Recurrent Abortion
  - Corticosteroid as a treatment.

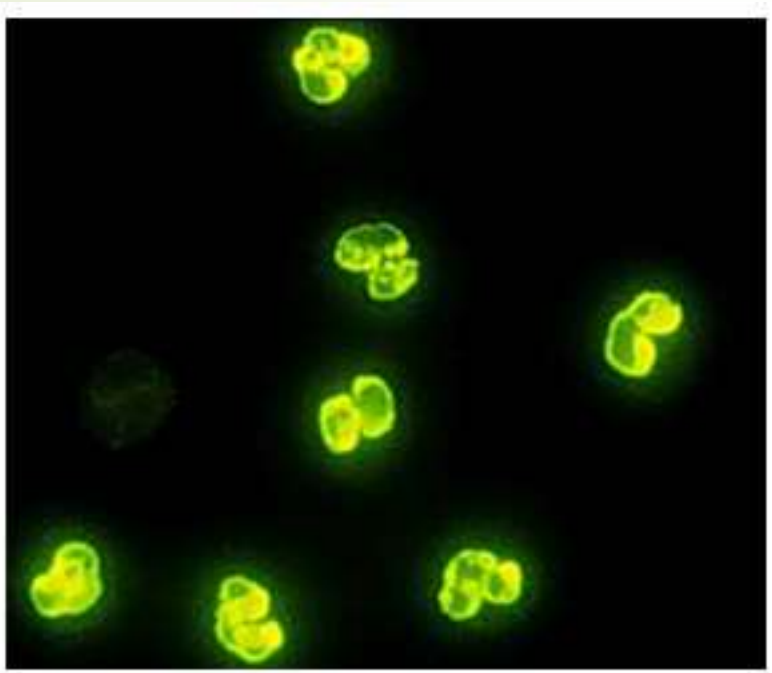
ANCA associated ⇒ No Immune complexes, why? Ab attacks Neutrophils.

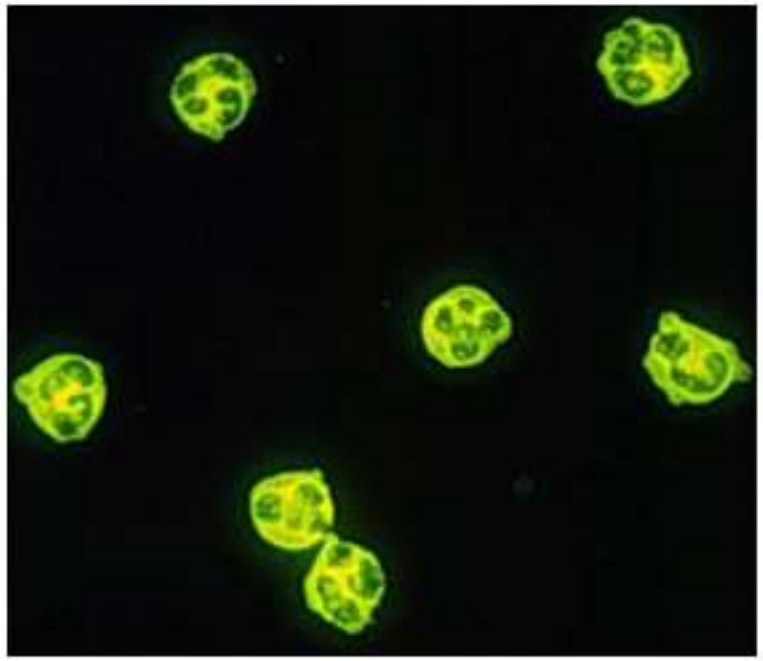
- Patients have circulating antibodies react with neutrophil cytoplasmic antigens *(antineutrophil cytoplasmic antibodies (ANCAs)*.
- ANCAs are a heterogeneous group of autoantibodies directed against constituents (usually enzymes) of neutrophil primary granules, monocyte lysosomes.
- Two main patterns are recognized by IF studies:

1. **Cytoplasmic** localization of the staining (c-ANCA), target antigen is proteinase-3 (PR3), a neutrophil granule constituent. *(Anti-proteinase-3)* → **granulomatosis with polyangiitis**
2. **Perinuclear** staining (p-ANCA) & target antigen is myeloperoxidase (MPO). *(Anti-myeloperoxidase)* ***microscopic polyangiitis & Churg-Strauss syndrome***

ANCA associated

These auto-antibodies are directed against cellular constituents without circulating immune complexes. Lesion does not contain antibody and complement; so often described as "**pauci-immune**."





P-ANCA Pattern — C-ANCA Pattern

Ab in Perinuclear Location

الجوز في Neutrophils

Ab in Cytoplasm

Anti-Endothelial Cell Antibodies & Autoreactive T Cells

- Antibodies to ECs underlie certain vasculitides, such as **Kawasaki disease**
- Autoreactive T cells cause injury in some forms of vasculitides characterized by formation of granulomas.

Classification of Vasculitis

Vessel	Disease	summary
Large	Giant-cell arteritis	F, >50. Arteries of head.
	Takayasu arteritis	F, <40. "Pulseless disease"
Medium	Polyarteritis nodosa	Young adults. Widespread.
	Kawasaki disease	<4. Coronary disease. Lymph nodes.
Small	Wegener granulomatosis	Lung, kidney. c-ANCA.
	Churg-Strauss syndrome	Lung. Eosinophils. Asthma. p-ANCA.
	Microscopic polyangiitis	Lung, kidney. p-ANCA.

Temporal (giant cell, cranial) arteritis

- A **chronic inflammatory disorder** affects principally **large- to small-sized arteries in the head (**the temporal, vertebral, ophthalmic arteries**)**, also affect the aorta, & may cause thoracic aortic aneurysm.
- It is the most common form of vasculitis among older adults in developed countries.
- Ophthalmic arterial involvement may lead to permanent blindness. Therefore, giant cell arteritis is a medical emergency that requires prompt recognition & treatment.

Temporal (giant cell, cranial) arteritis

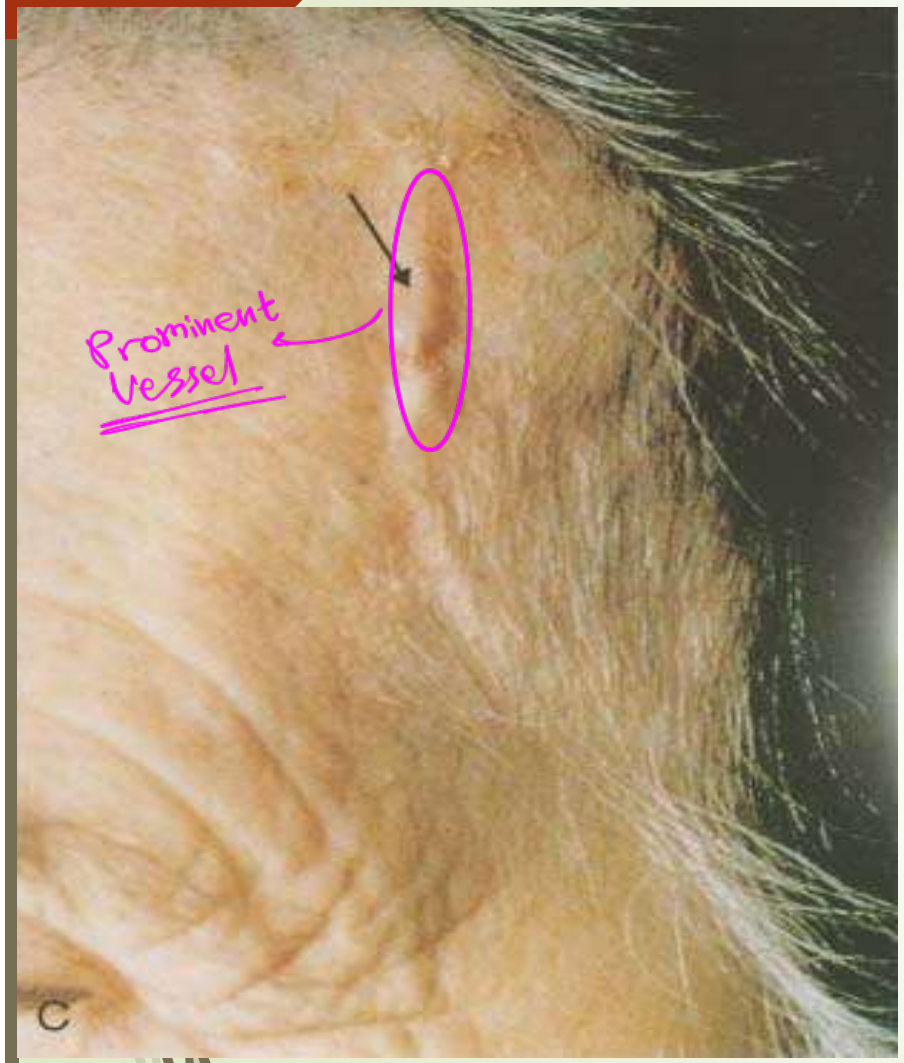
- **Histology**
  - granulomatous inflammation
  - chronic non-specific panarteritis
  - fragmentation of the internal elastic lamina
    - ↳ Destruction
- **Pathogenesis**
  - T Cell mediated immunity

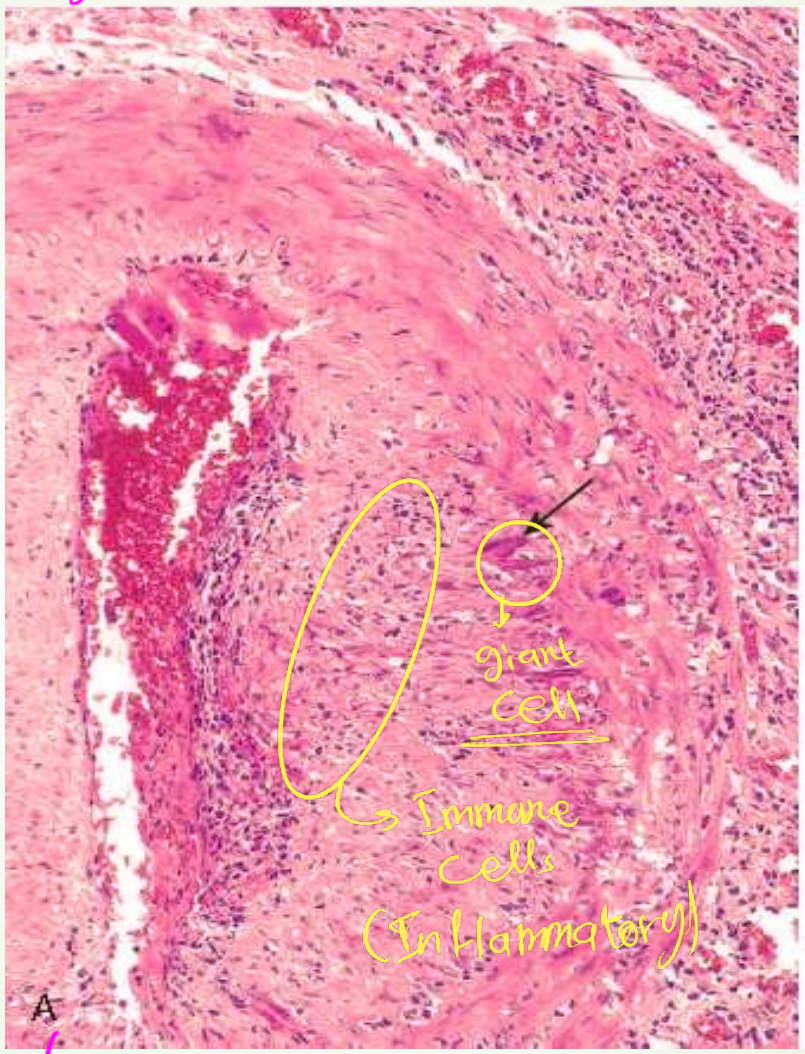
Temporal (giant cell, cranial) arteritis

- **Clinical features**
  - Females > males (~X4)
  - > 50 years (rare before 50 years of age)
  - non-specific constitutional symptoms
  - Headache, local facial pain & tenderness
  - ocular symptoms, 50 % (range from diplopia to blindness)
- **Diagnosis**
  - Biopsy (at least 1cm)→ Could be negative (very focal involvement)
  - Rx: corticosteroids are effective.

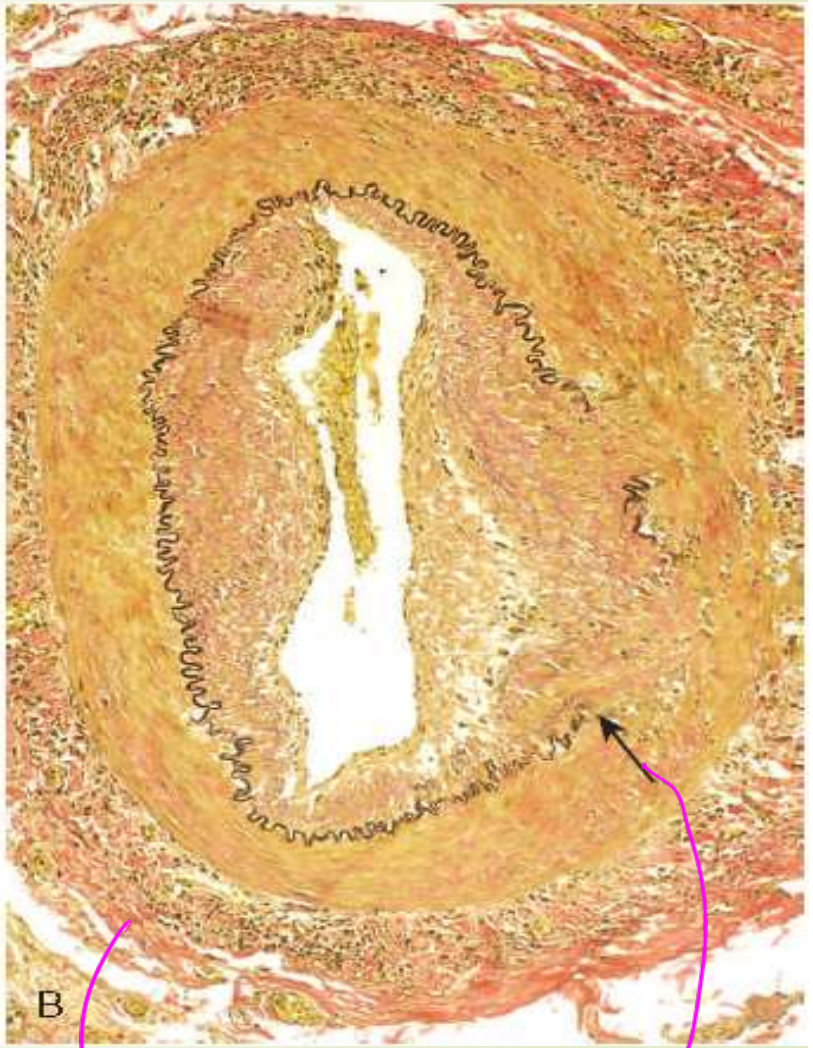
Mostly affected → females
↑ 50 yrs

Presentation? Headache !! along w/ ophthalmic symptom → diplopia
→ blurred vision

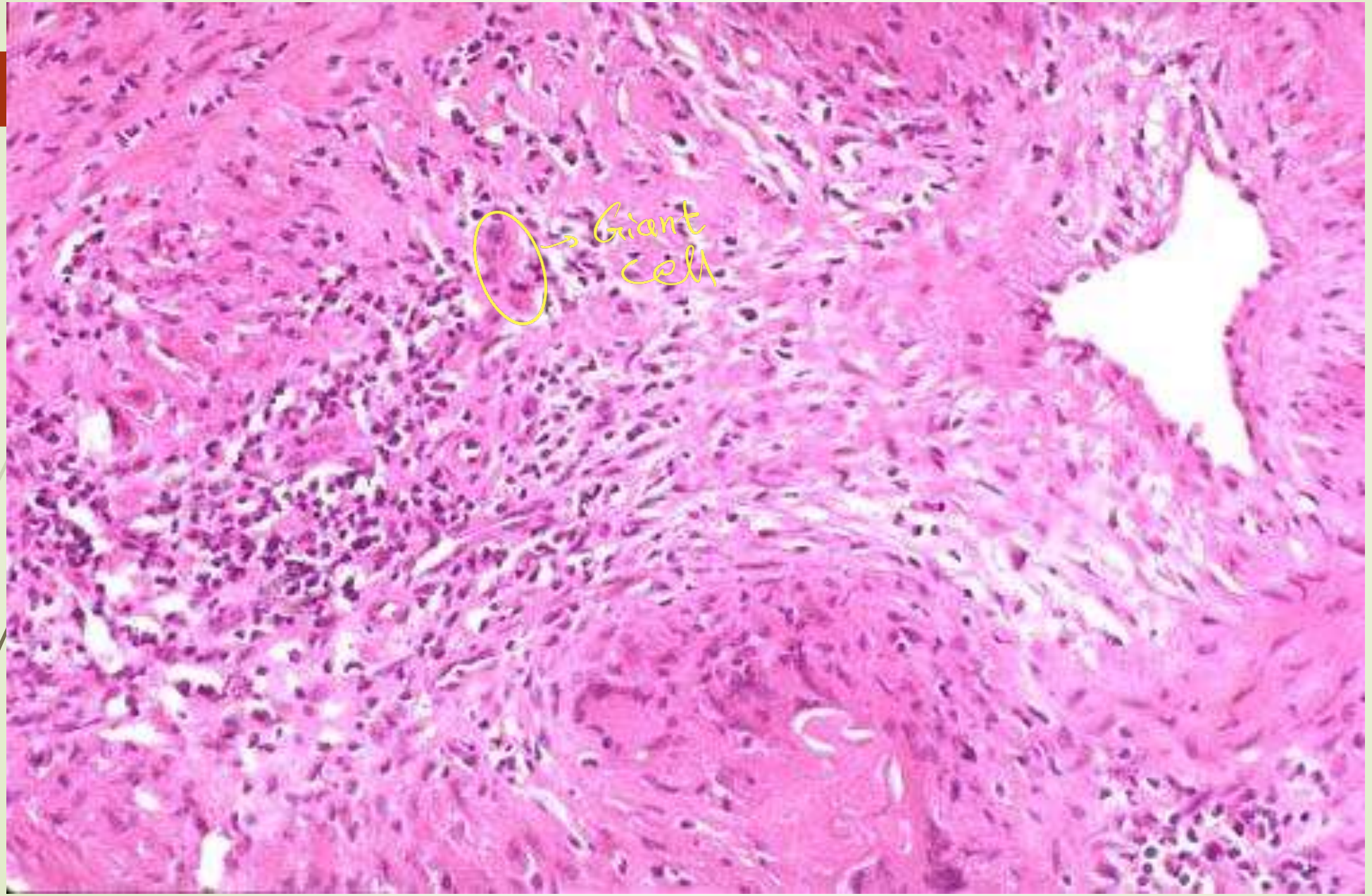




Biopsy?
More than 1cm



elastic stain, highlight elastic
Destruction of elastic layer!


Giant cell

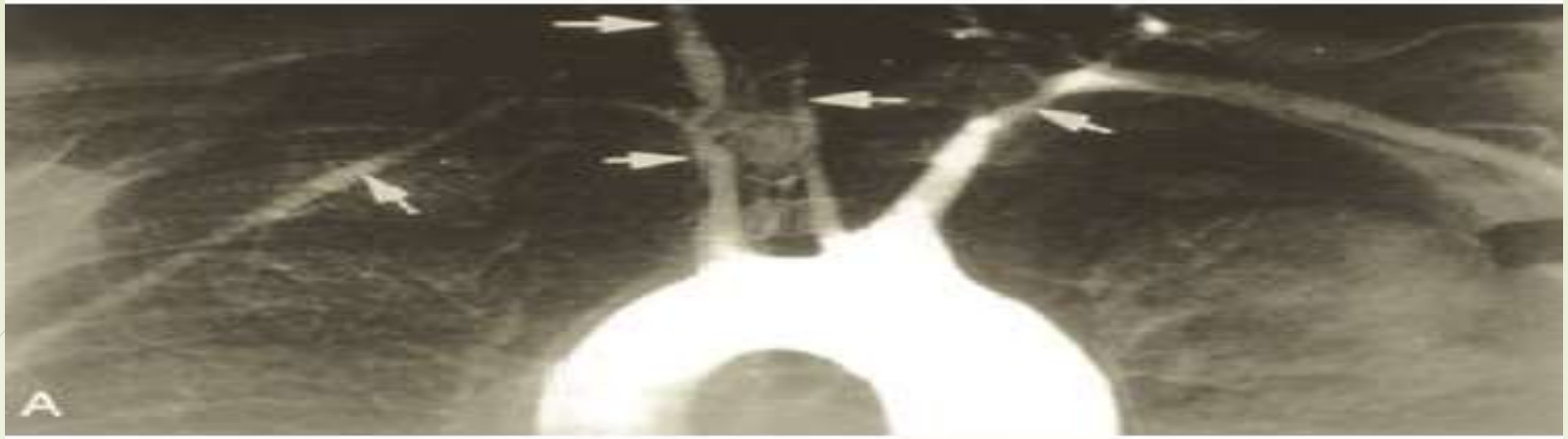
Takayasu Arteritis (pulseless disease)

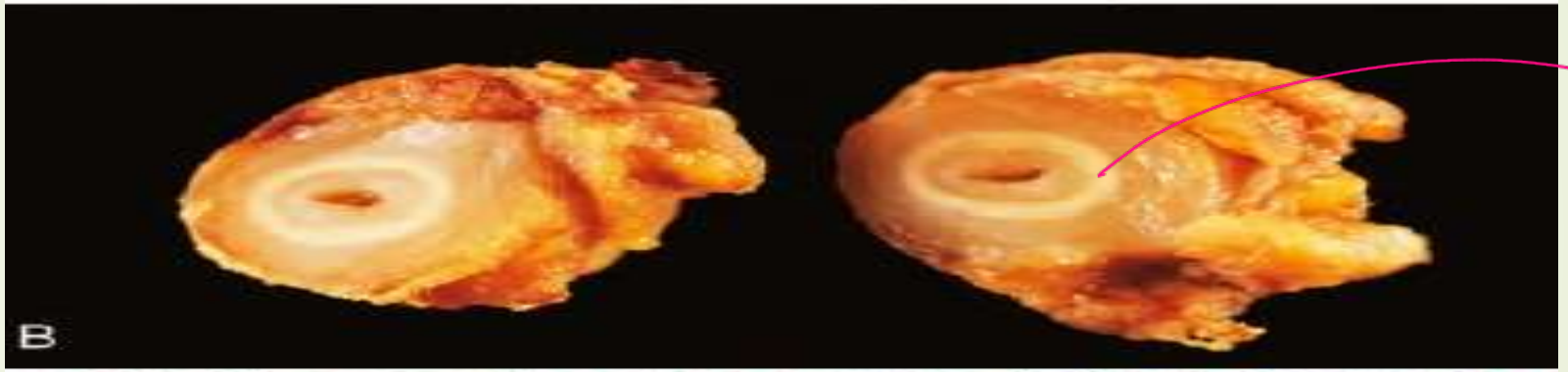
Japanese Women
↓40 yrs
Main characteristic → Affect Aotic arch
↓
Narrowing
+
Weak pulse in upper limb

- A granulomatous vasculitis of **medium & larger** arteries affects mainly arch of aorta.
- Characterized by transmural fibrous thickening & obliteration of aortic arch & great vessels → luminal narrowing of the major branch vessels → the origin of great vessels.
- Symptoms are secondary to luminal narrowing:

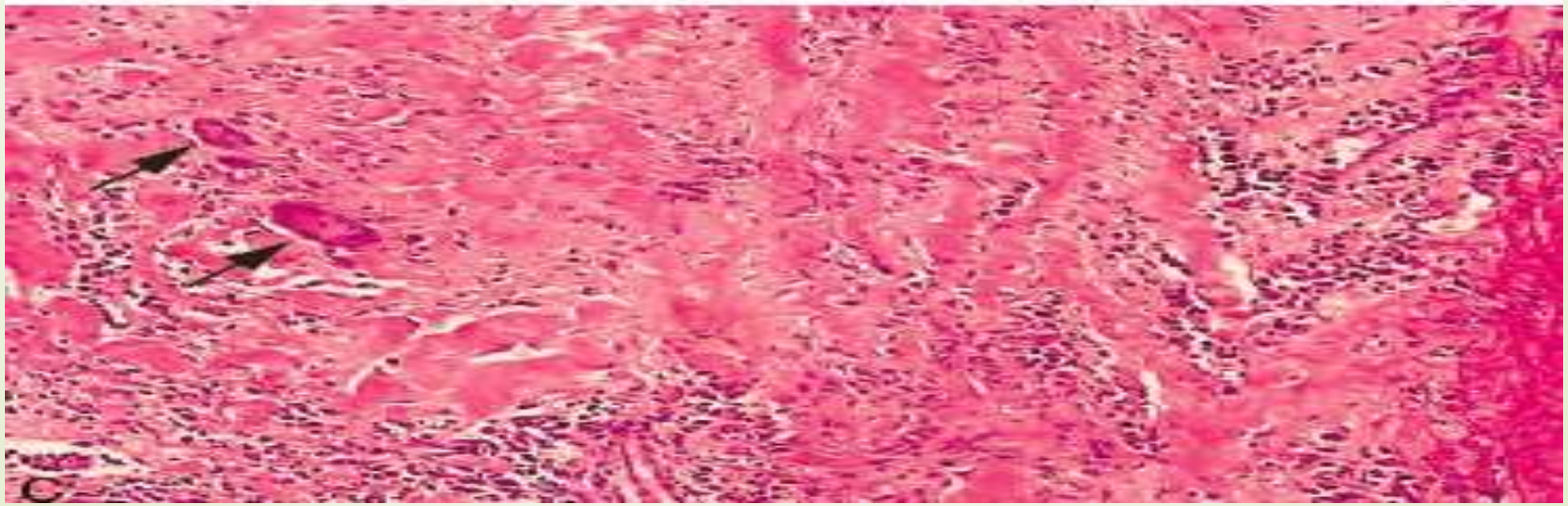
ocular disturbances & marked weakening of the pulses in the upper extremities →(pulseless disease).

- More common in females younger than 40 years and more frequently in Asian countries.
- Course of disease is variable ,may enter in quiescent stage.





Marked thickening



Polyarteritis nodosa (PAN)

Not involve Pulmonary!

Related to Necrosis → Transmural inflammation. "Necrotizing"

- A systemic disease characterized by necrotizing inflammation of **small - to medium - sized arteries** throughout the body (renal and visceral), sparing the pulmonary circulation.
- The involvement of the vessels is **focal, random & episodic.**
- It often produces irregular aneurysmal **dilatation (coz it weakens the arterial wall)** nodularity, and vascular **obstruction leading to infarctions.**
- Acute lesions show **segmental transmural necrotizing inflammation** extending around the vessel.

→ Associated w/ hemeturia, blood in urine.

Polyarteritis nodosa (PAN)

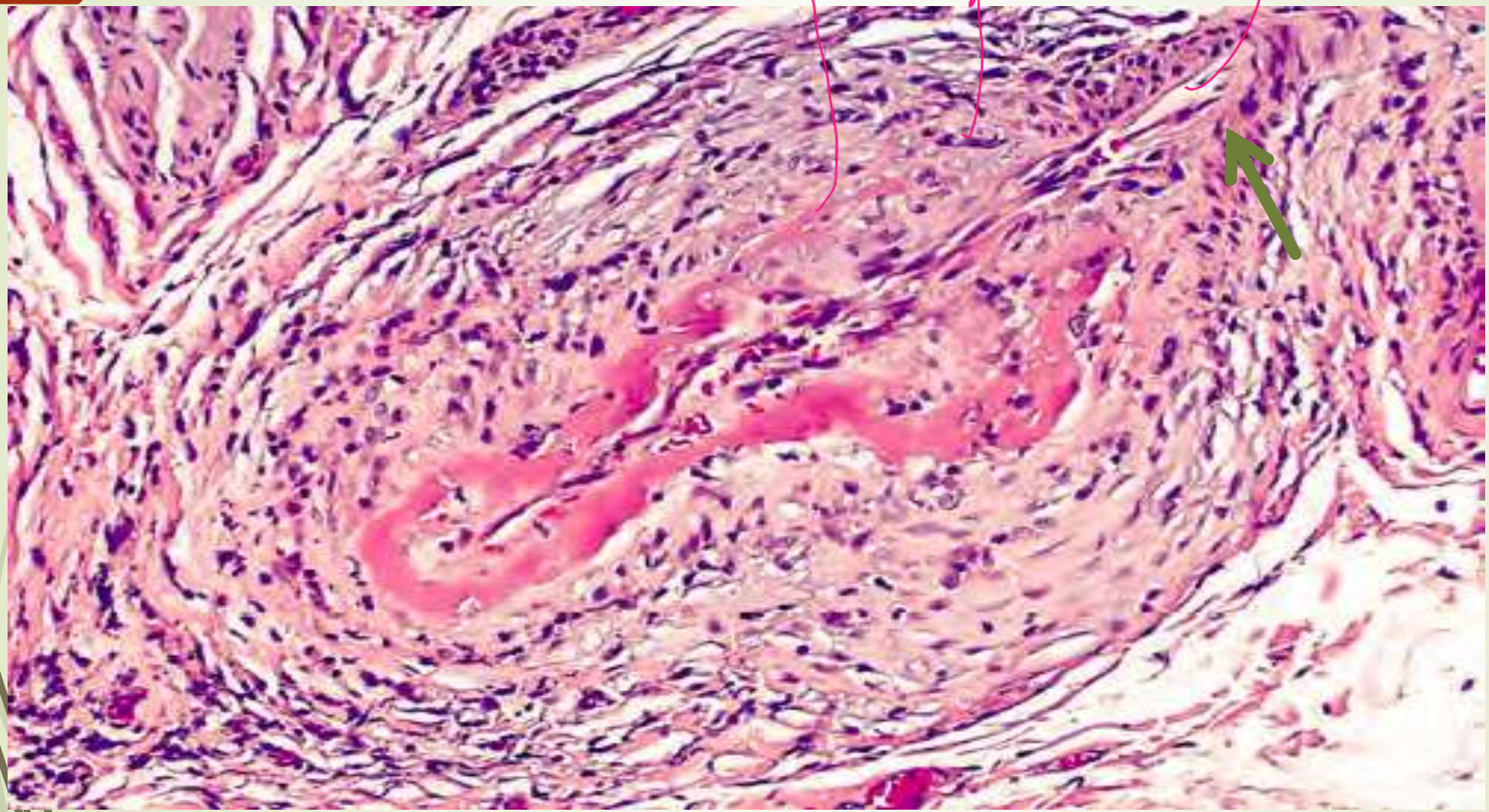
Episodic (Intermittent)

I could see both stages (Healed, Active) in same BT !!

- Healed lesions show marked fibrotic thickening of the arterial wall , with associated elastic lamina fragmentation.
- All stages of activity may coexist in different vessels or even in the same vessel and this is so characteristic of PAN → ongoing and recurrent insults.
- Clinical features

young adults, males > females , vascular involvement is widely scattered → clinical picture can be varied & puzzling.

- Diagnosis .... Biopsy
- Rx … immunosuppression


Necrosis
Neutrophils
Destructive Endothelial

Kawasaki disease (mucocutaneous lymph node syndrome)

- Acute febrile illness, **large- to medium-sized vasculitis** of infants & children (< 4 years) characterized by
  - Fever,
  - Lymphadenopathy,
  - Skin rash
  - Oral / conjunctival erythema.
- 20% have coronary vasculitis ,often with aneurysm.
- Histology like PAN → Necrosis, Elastic fragmentation, ↑ Inflammatory cells.
- Etiology ; unknown (auto-antibodies to ECs)
- Self-limited disease, rarely fatal(1%) → complications of coronary involvement.

Granulomatosis With Polyangiitis

- Previously called *Wegener granulomatosis.* "fatal"
- Classical cases consist of a triad:
  1. Granulomatous or necrotizing vasculitis mainly in the **lung** & upper respiratory tract.
  2. Necrotizing granulomas of upper &/or lower respiratory tract
  3. Renal involvement
     - focal necrotizing glomerulonephritis
     - rapidlly progressive glomerulonephritis → if not treated? Renal failure.
- Clinical picture
  - overlaps with PAN
  - Males > females, peak at 5th decade

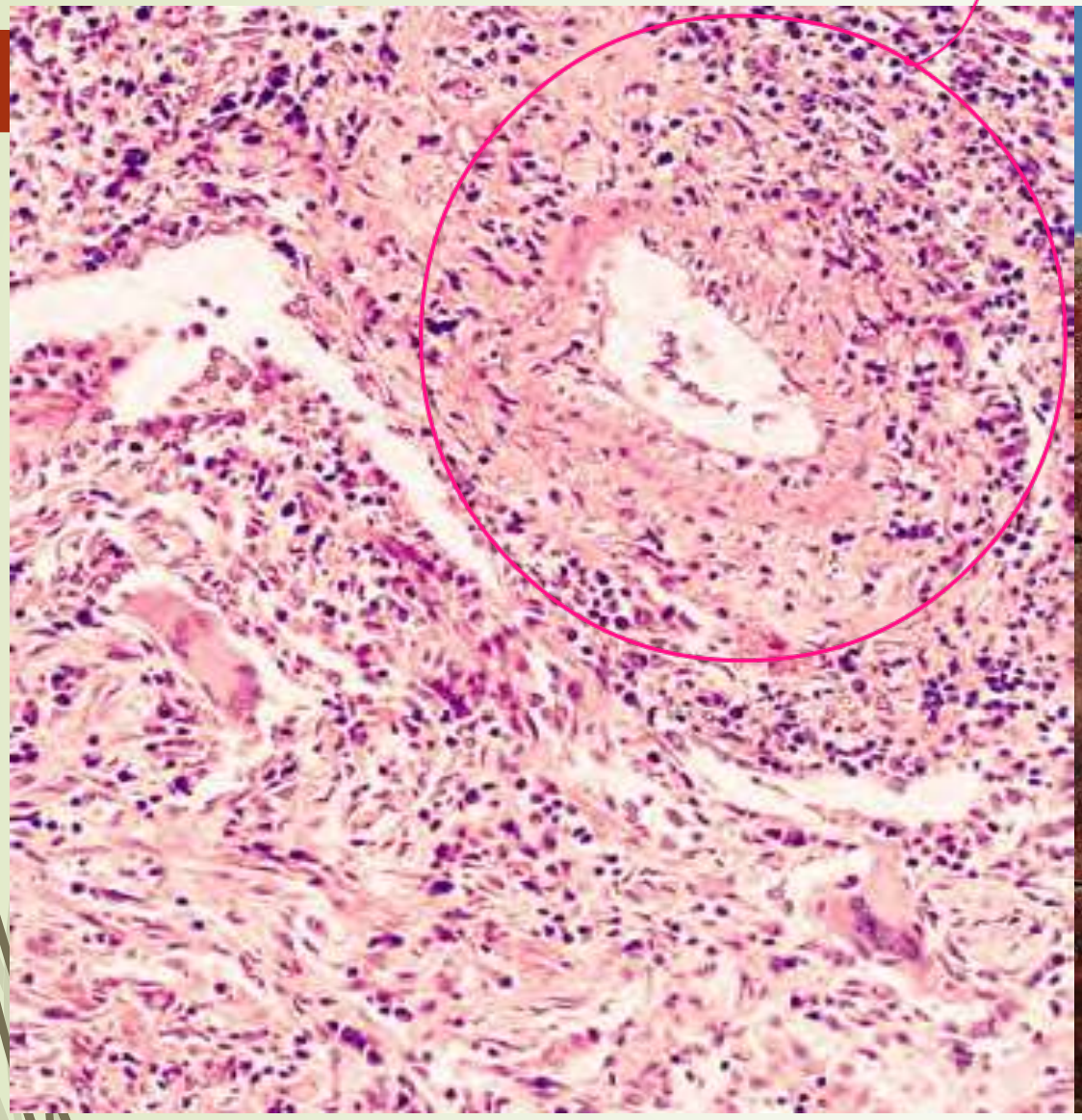
Hemeturia + Hemoptysis → symptoms

Granulomatosis With Polyangiitis

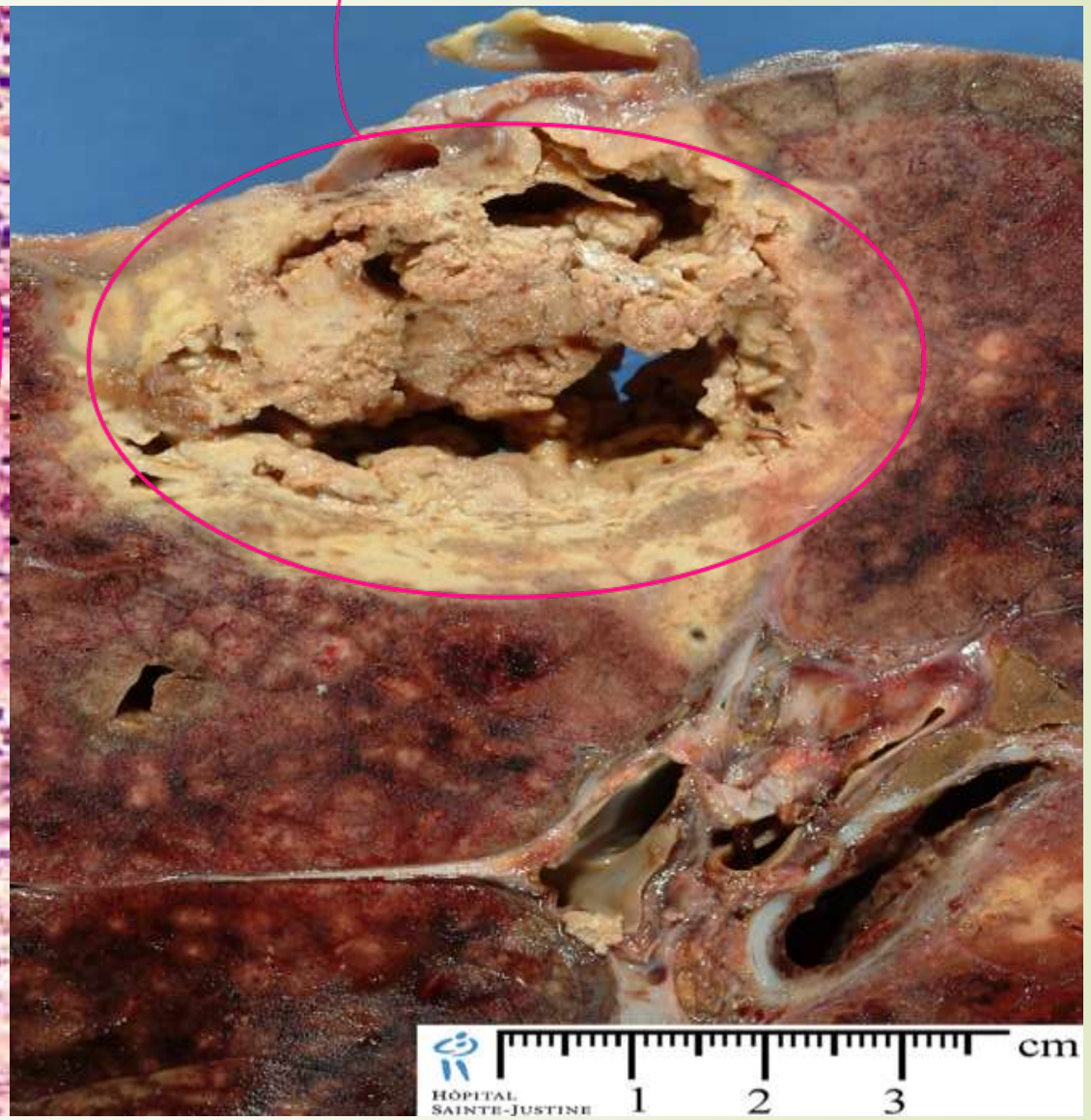
- Diagnosis
  - Lung biopsy, kidney biopsy, or nasal biopsy,
- Prognosis
  - 80% die within a year (if not treated)
  - 90% respond to treatment
- Pathogenesis
  - T Cell Mediated.
  - > 95% PR3-ANC positive (Mirrors the clinical coarse)

$R_x \rightarrow$ Plasmea pharesis Immediately

Numerous chronic Infl. cells, giant cell granuloma



Necrosis

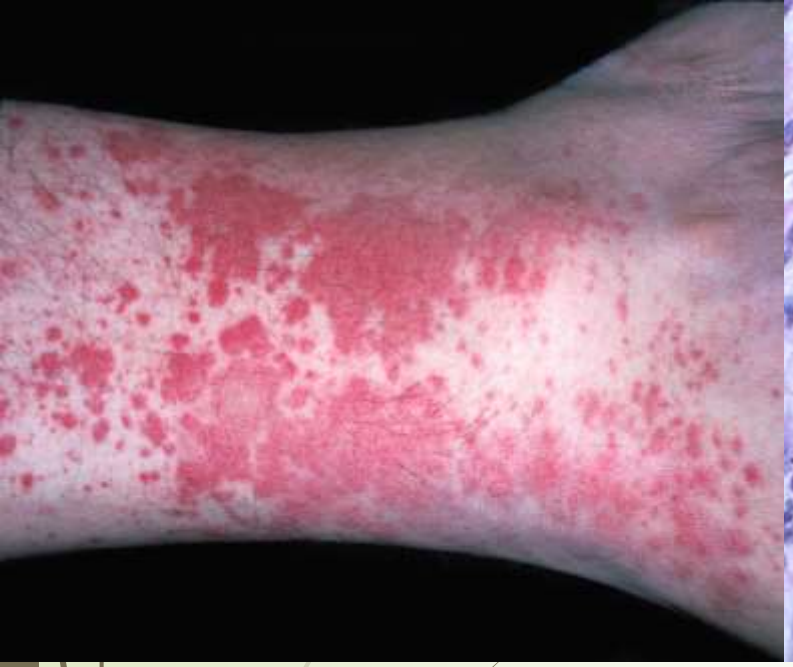


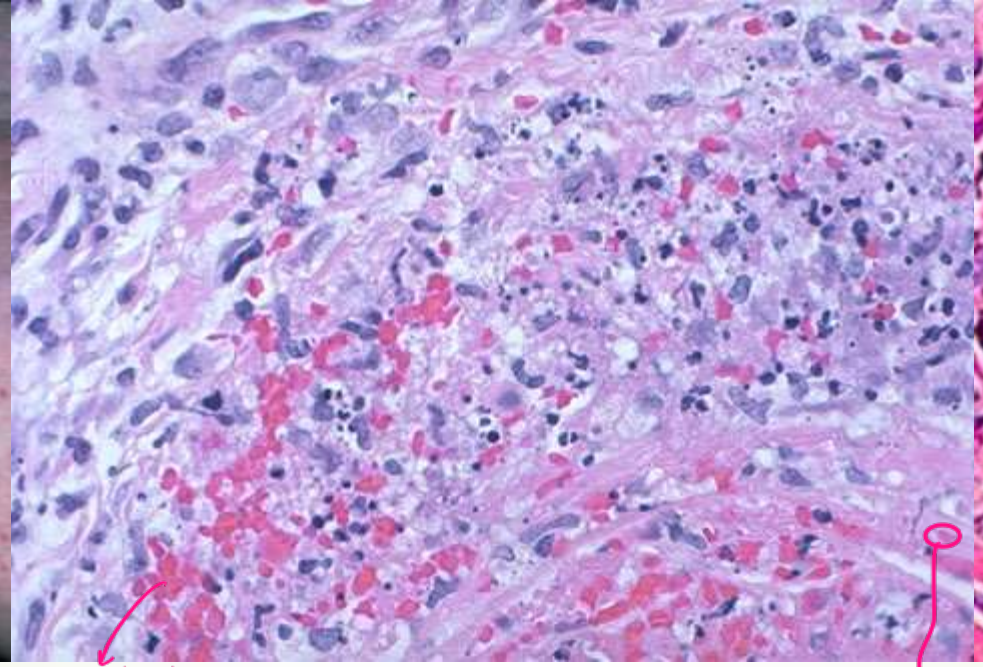
small BV

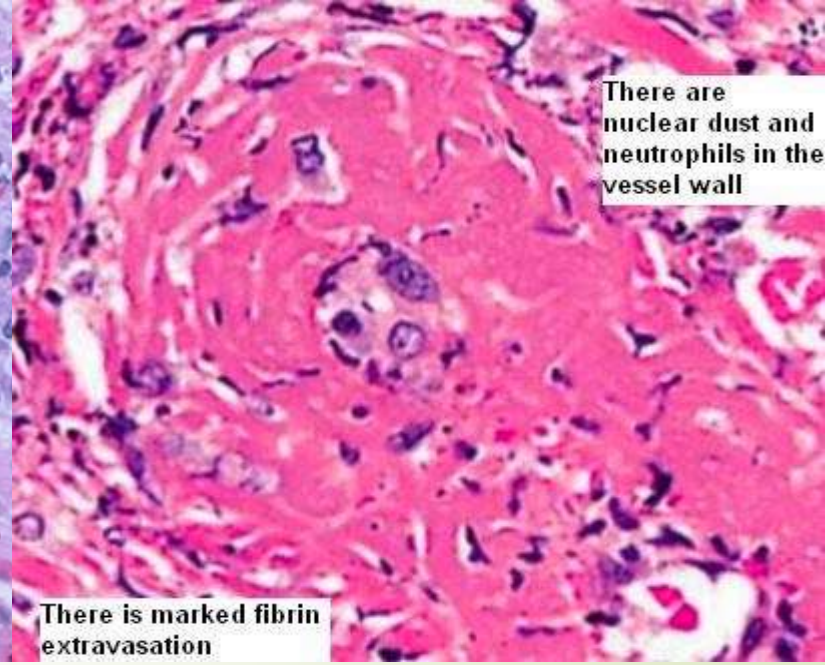
Microscopic polyangiitis (microscopic polyarteritis)
or
HYPERSENSITIVITY vasculitis
OR
LEUKOCYTOCLASTIC vasculitis

Most cases of microscopic polyangiitis are associated with MPO-ANCA , Although immunoglobulins and complement components can be demonstrated in early skin lesions, most lesions are "pauci-immune"

No Immune complexes, related to P-ANCA / C-ANCA







- Involvement of small vessels (arterioles, capillaries, & venules).
- all lesions of the same stage/age.
- Skin, mucous membranes, lungs, brain, heart, GIT, kidney & muscles.

In contrast to PAN, necrotizing glomerulonephritis (90%) & pulmonary capillaritis are common

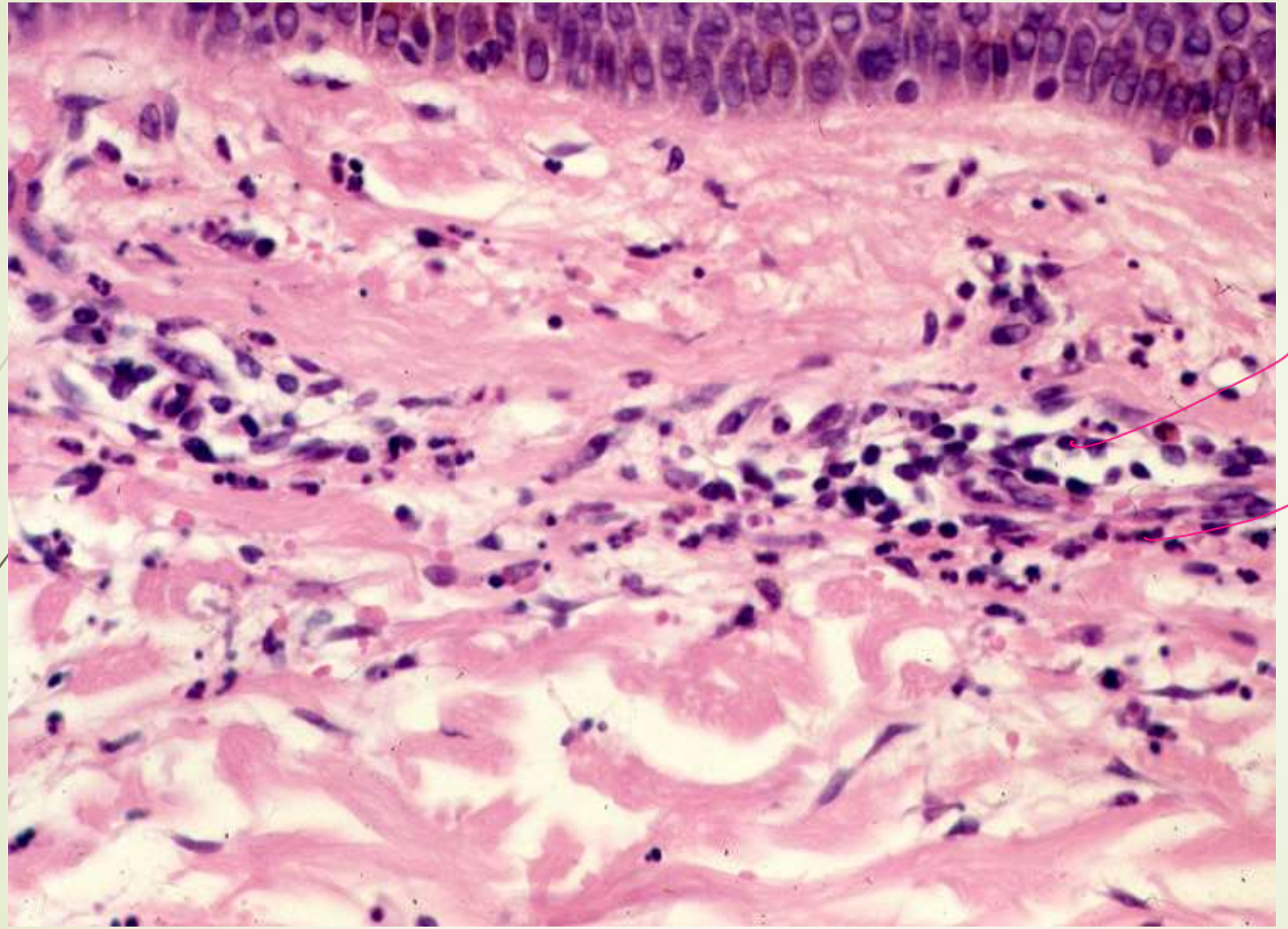
الأعراض تعتمد على العضو ⊛

Same microscopic + Age

- Segmental fibrinoid necrosis of media.
- No granulomatous inflammation
- Sometimes limited to infiltration of vessel wall by neutrophils with **nuclear fragmentation (leucocytoclasia), leukocytoclasatic vasculitis.**
- A reaction to an Ag such as drugs, microorganisms or hetrologous protein in a previously sensitized patients.

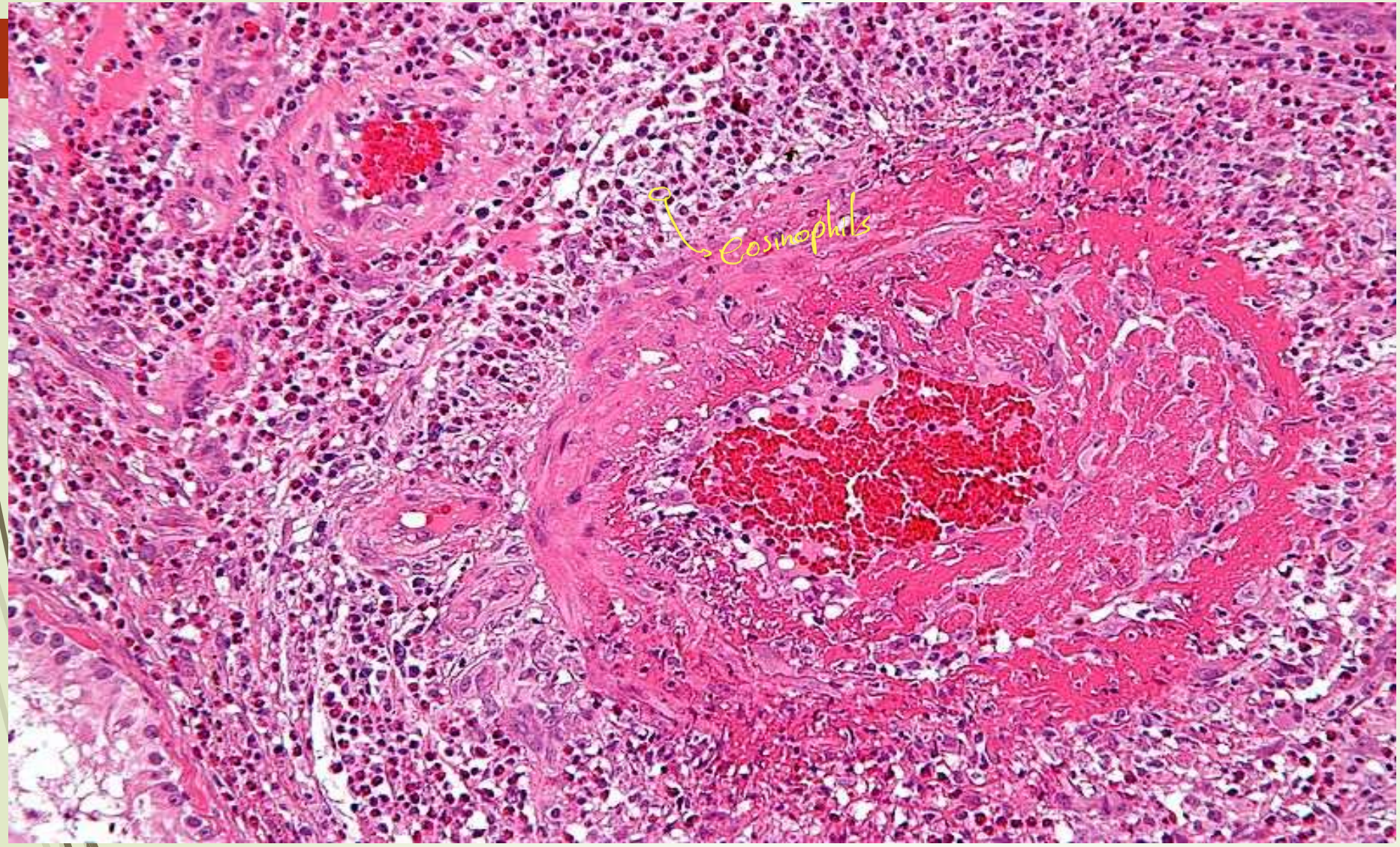
Clinical: hemoptysis, arthralgia, abdominal pain, hematuria, proteinuria, hemorrhage, & muscle pain or weakness.

- Except in brain or renal involvement most patients respond to removal of offending antigens & immunosuppression.
- Ass : Henoch -schonlein purpura (HSP), essential mixed cryoglobulinemia, vasculitis with malignancy


Nuclear Fragmentation
Neutrophils

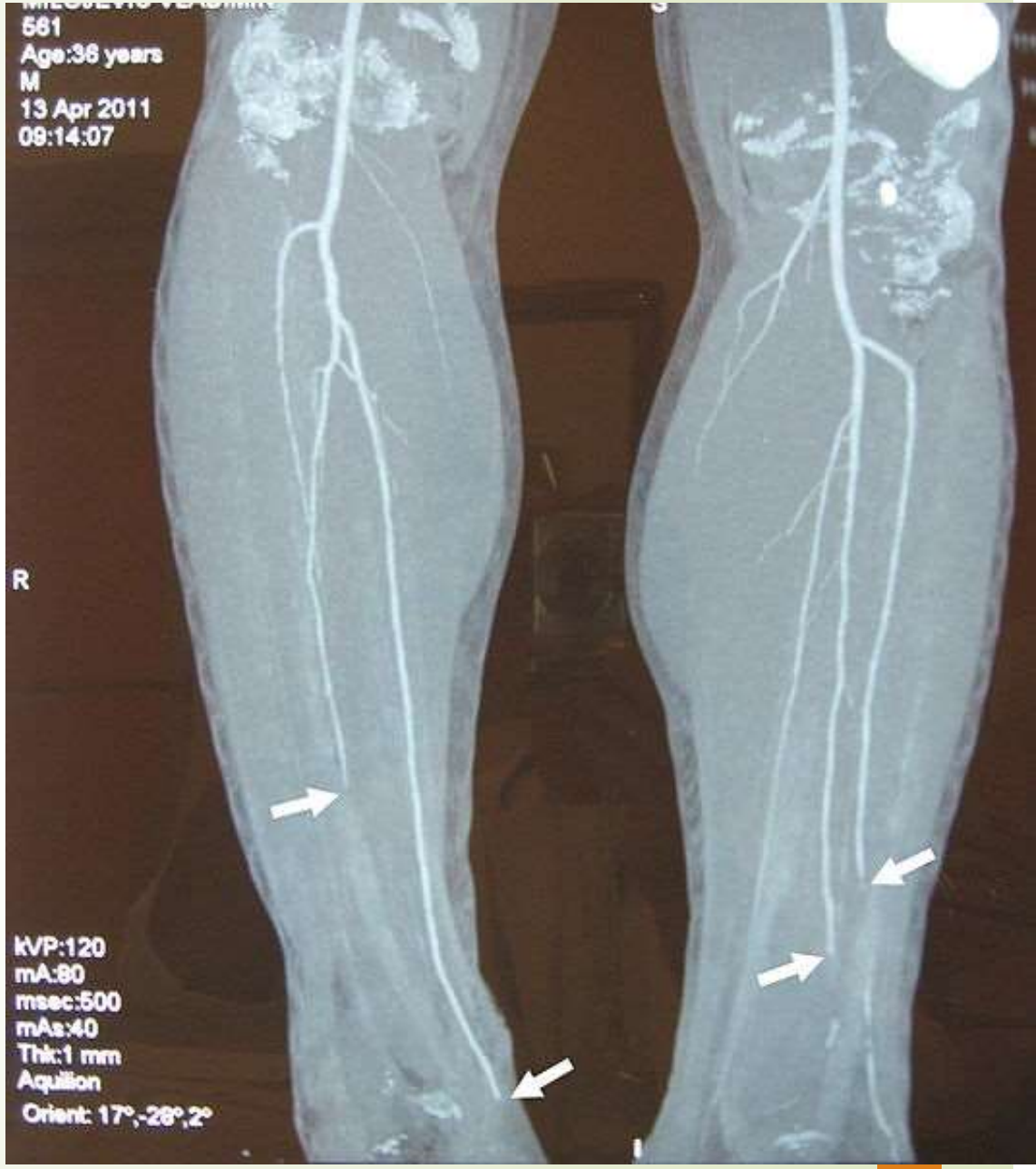
In allergic granulomatosis and angiitis (Churg-Strauss syndrome)

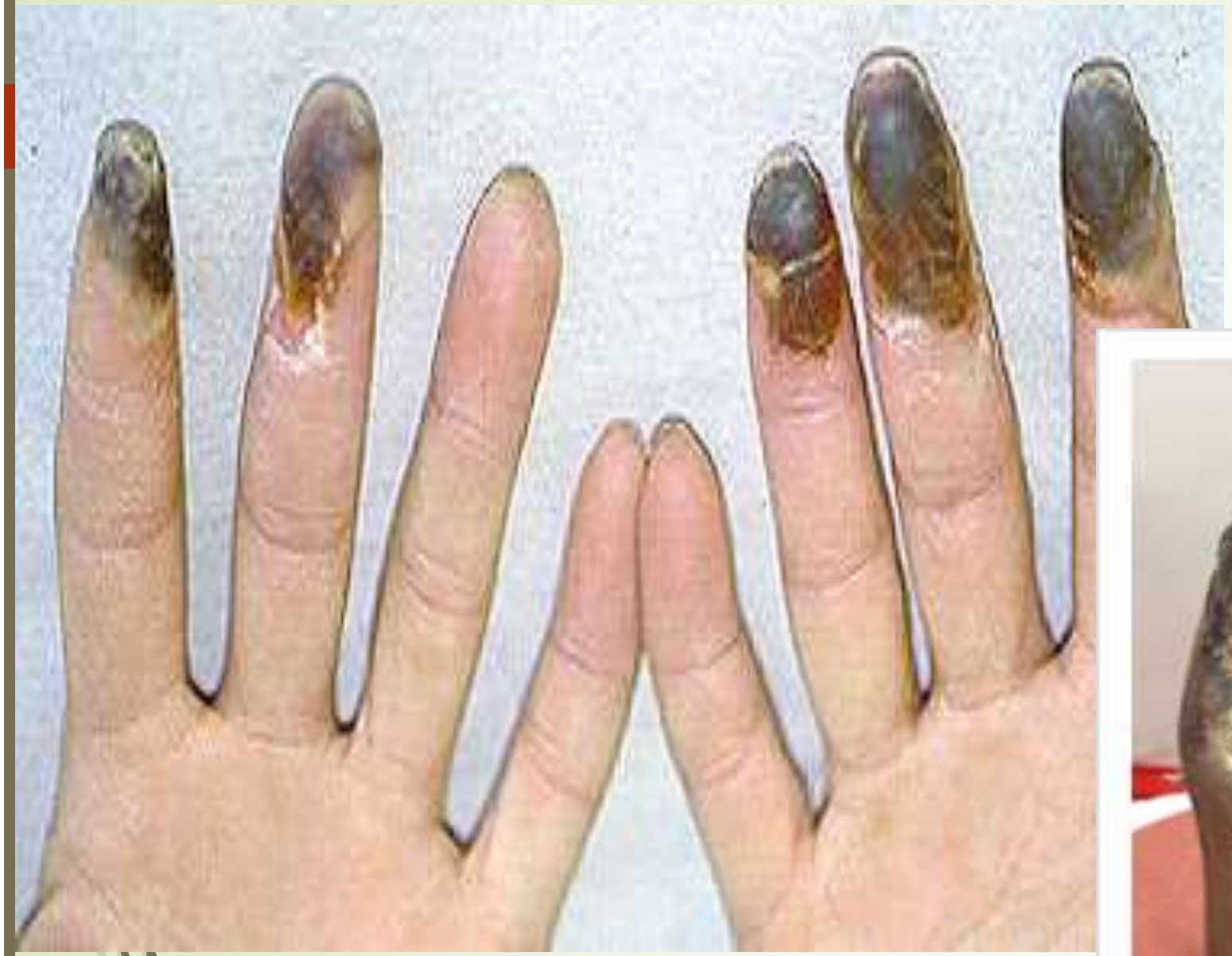
- Rare disease characterized by
  - necrotizing vasculitis accompanied by granulomas with **eosinophilic** necrosis.
  - p-ANCAs are present in A minority of patients.
  - There is a strong association with allergic rhinitis, bronchial asthma, and peripheral eosinophilia.
  - Coronary arteritis & myocarditis are the principal causes of morbidity and mortality.


Eosinophils

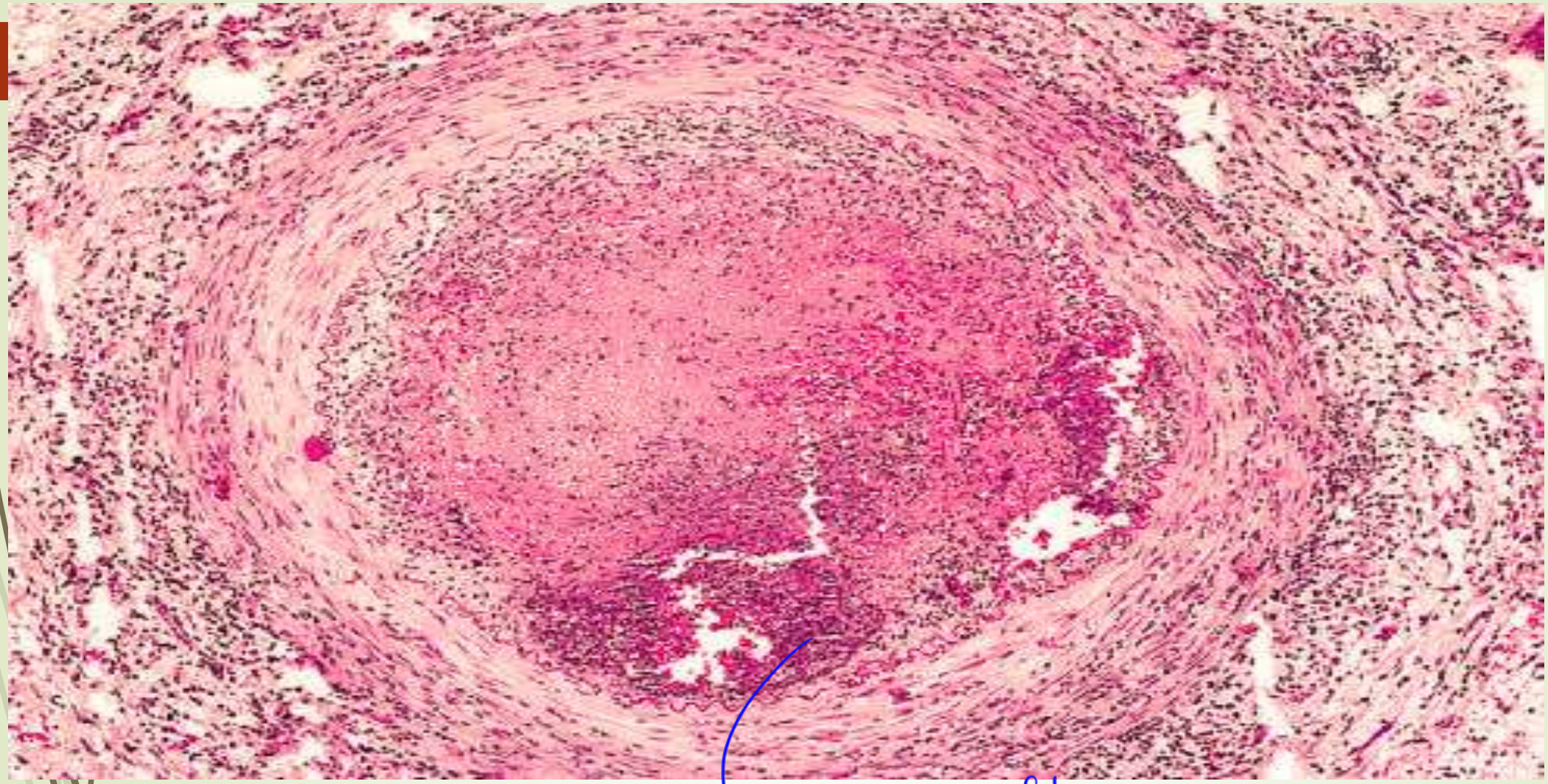
Thromboangiitis obliterans (Buerger's Disease)

- A condition marked by segmental, **thrombosing**, acute & chronic inflammation of intermediate & small arteries & veins in the limbs with extension to accompanying nerves.
- Exclusively seen in heavy smokers males before the age of 35.
- Instep claudication followed by pain at rest, might end in gangrene.
- Etiology ? Endothelial cell injury by toxins in tobacco.





Gangrenes


Thrombosis
fibrin
RBC
platelets