

# Vasculitis

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**Reference: Robbins & Cotran Pathology and Rubin's Pathology**

## **Objectives: At the end of this lecture, the student should:**

- Know the common causes of vasculitis with special emphasis on the clinic-pathological features and mechanism of: Giant cell arteritis. Polyarteritis nodosa. Wegener's granulomatosis. Cutaneous hypersensitivity vasculitis. Thromboangiitis obliterans (Burger's disease)

### **Key principles to be discussed:**

- Pathology of vasculitis: giant cell arteritis, polyarteritis nodosa, Wegener's granulomatosis and cutaneous hypersensitivity vasculitis.
- **Key principles to be reviewed by self-teaching (additional reading):**  
Henoch Schonlein purpura

# Lecture outline

- Giant cell arteritis.
- Polyarteritis nodosa.
- Wegener's granulomatosis.
- Cutaneous hypersensitivity vasculitis and Henoch Schonlein purpura.
- Thromboangiitis obliterans (Burger's disease)

# Vasculitis

It is inflammation of vessel walls with many possible symptoms

## Causes:

1. It is usually immune-mediated
  - ❖ Immune complex deposition
  - ❖ Antineutrophil cytoplasmic antibodies (ANCA)
  - ❖ Anti-endothelial cell antibodies
  - ❖ Autoreactive T cells
2. It can also be caused by infection, physical or chemical injury

# **Giant-Cell (Temporal) Arteritis**

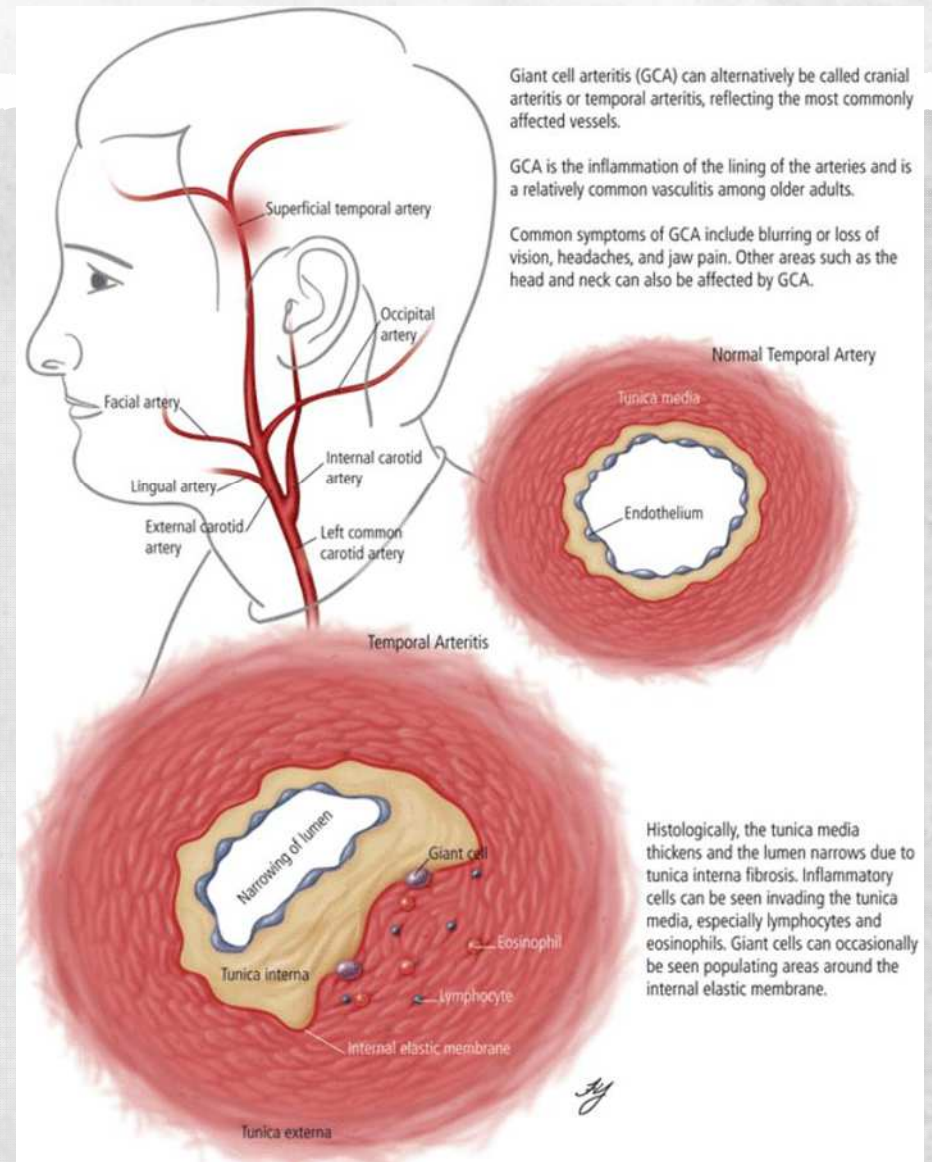
## Giant-Cell (Temporal) Arteritis

- ▶ Most common type of vasculitis
- ▶ Patients more than 50yrs of age
- ▶ Female: Male = 2:1.
- ▶ Chronic, granulomatous inflammation of large to medium sized arteries, especially the branches of the carotid artery in the head (temporal artery and branches of the ophthalmic artery)
- ▶ Involvement is segmental, acute and chronic.



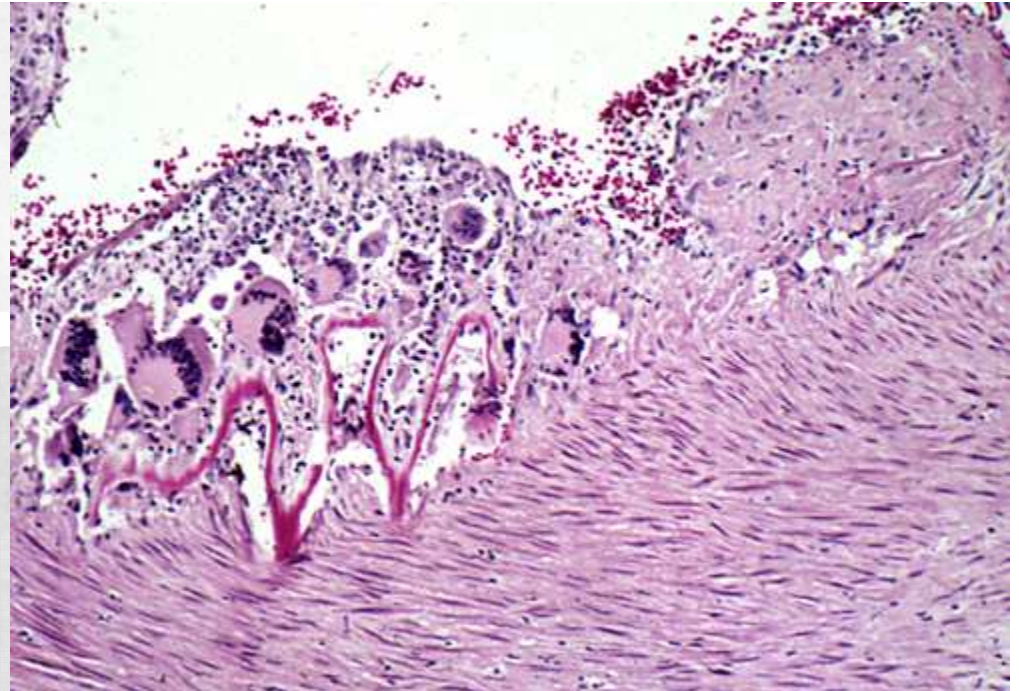
# Giant-Cell (Temporal) Arteritis: Clinical Features

- Symptoms :
  - ✓ fever, facial pain or headache, often most intense along the course of the superficial temporal artery,
  - ✓ Thickened and painful temporal artery
  - ✓ Jaw pain
  - ✓ Visual problems and acute vision loss
- The diagnosis depends on biopsy and histologic confirmation.
- Treatment: corticosteroids

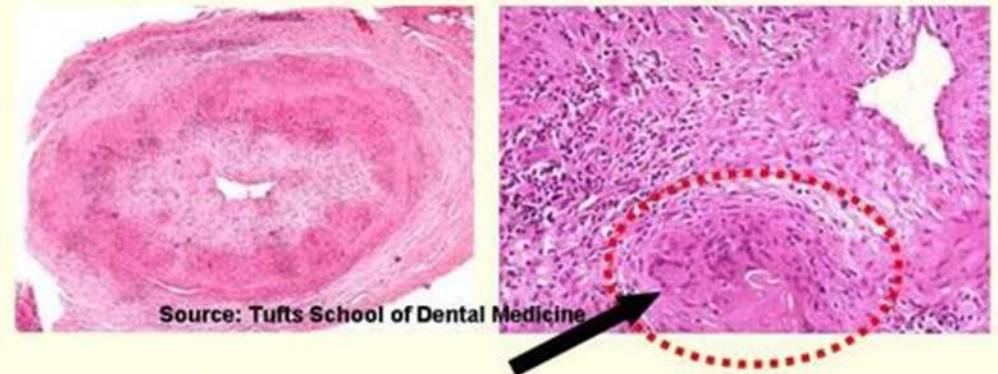


## Giant-Cell (Temporal) Arteritis: morphology

- Granulomatous inflammation of the blood vessel wall
- Giant cells
- Disruption and fragmentation of internal elastic lamina
- Proliferation of the intima with associated occlusion of the lumen.
- The healed stage reveals collagenous thickening of the vessel wall and the artery is transformed into a fibrous cord



Temporal Arteritis



Giant cells (arrow) within a granuloma (circle) of granulomatous inflammation



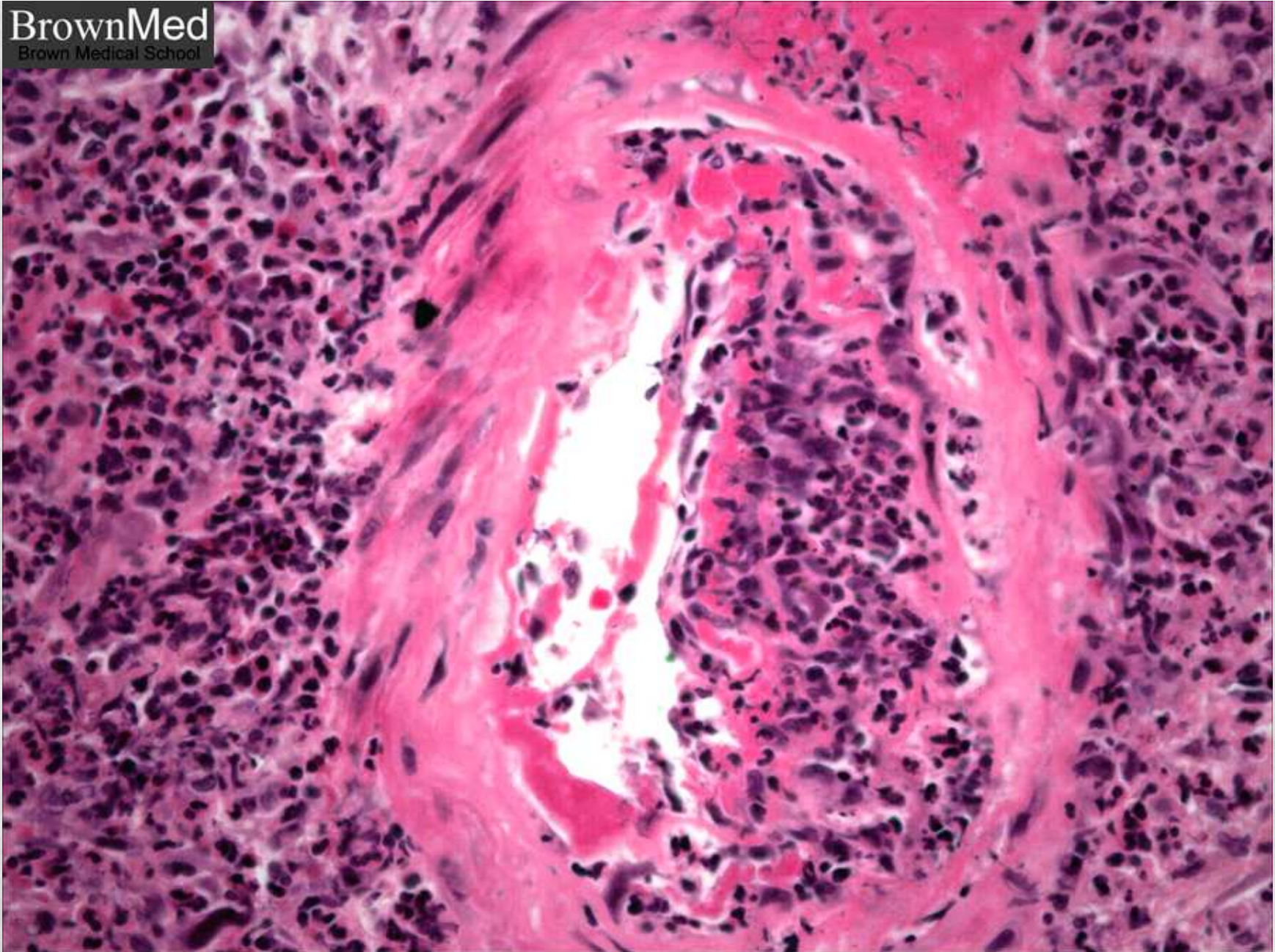
# **Polyarteritis Nodosa**

# Polyarteritis Nodosa

- Disease of young adults.
- **There is segmental necrotizing inflammation of arteries of medium to small size, in any organ except the lungs.**
- Most frequently kidneys (most common), heart, liver, and gastrointestinal tract.
- Polyarteritis nodosa has been associated with hepatitis B or hepatitis C virus infection.

## Clinical features

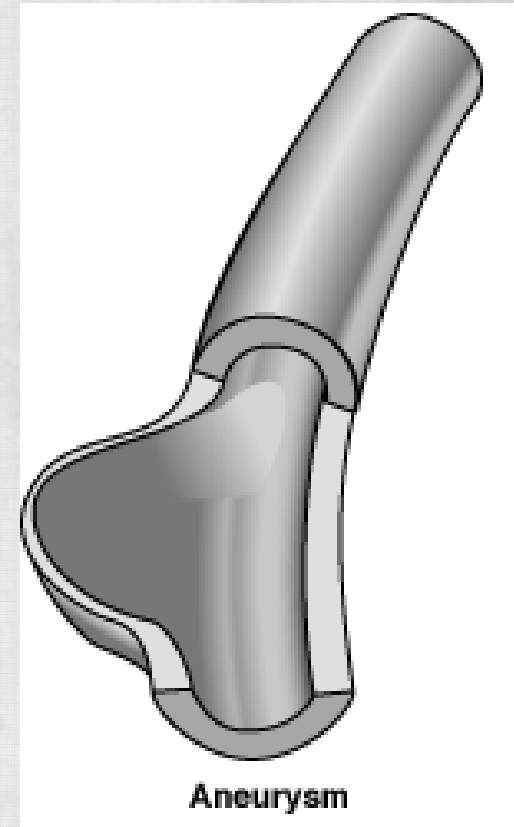
- Some clinical manifestations are due to ischemia and infarction of affected tissues/ organs.
- Fever, weight loss, abdominal pain and melena (bloody stool), muscular pain and neuritis.



Polyarteritis nodosa with segmental inflammation and fibrinoid necrosis and occlusion of the lumen of this artery. Note that part of the vessel wall at the left side is uninvolved.

# Polyarteritis Nodosa

- Weakening of the arterial wall due to the inflammatory process may cause aneurysmal dilation or localized rupture.
- Renal arterial involvement is often prominent and is a major cause of death.
- Particularly characteristic of PAN is that all the different stages of activity ( i.e. active and chronic stages) may coexist in same artery or in different artery at the same time.
- Fatal if untreated, but steroids and cyclophosphamide are curative.



# **Wegener granulomatosis**

# Wegener granulomatosis

is a type of necrotizing vasculitis characterized by the **triad** of

- 1) necrotizing granulomas** of the upper and lower respiratory tract
- 2) necrotizing or granulomatous vasculitis** of small to medium-sized vessels
- 3) renal disease** in the form of necrotizing, crescentic, glomerulonephritis.

# Wegener Granulomatosis

- Males are affected more often than females, at an average age of about 40 years
- C-ANCA (antineutrophilic cytoplasmic antibodies) is positive in serum of more than 95% of patients.
- Persistent pneumonitis, chronic sinusitis, mucosal ulcerations of the nasopharynx, and evidence of renal disease.
- Untreated: fatal - may lead to death within 2 years if not treated.



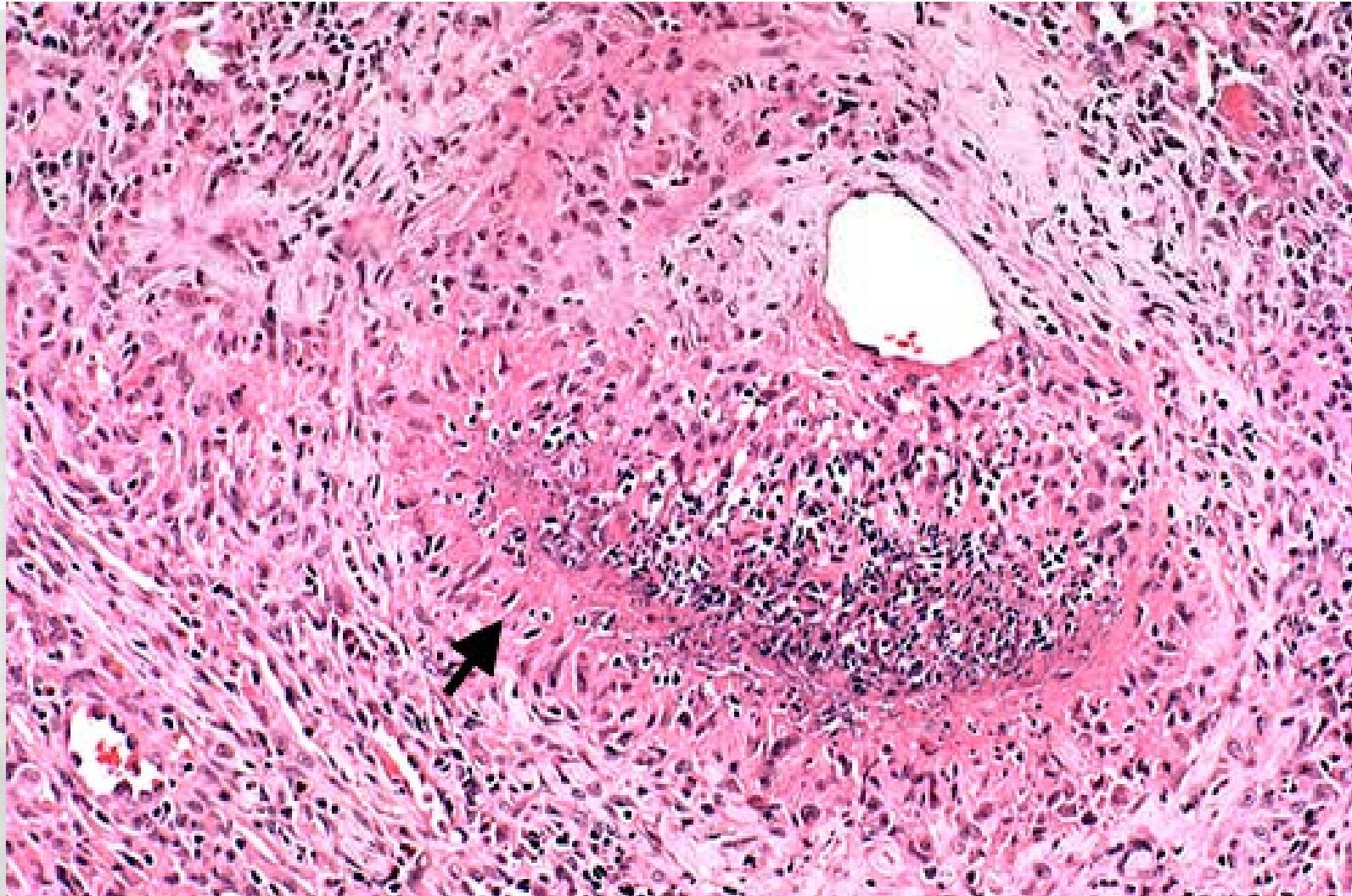
Wegener granulomatosis: palatal ulceration



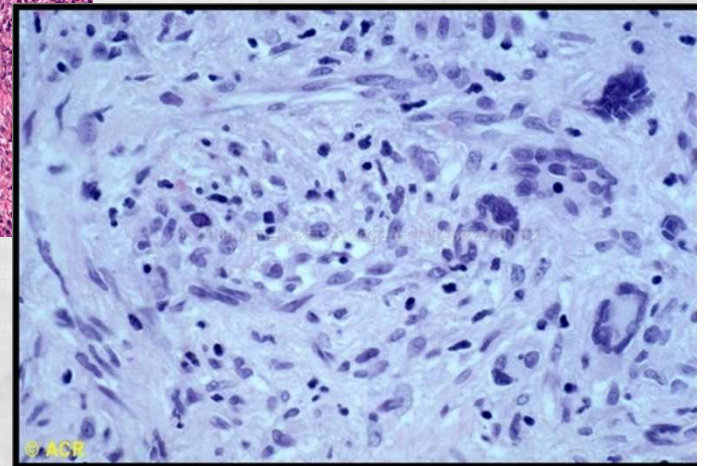
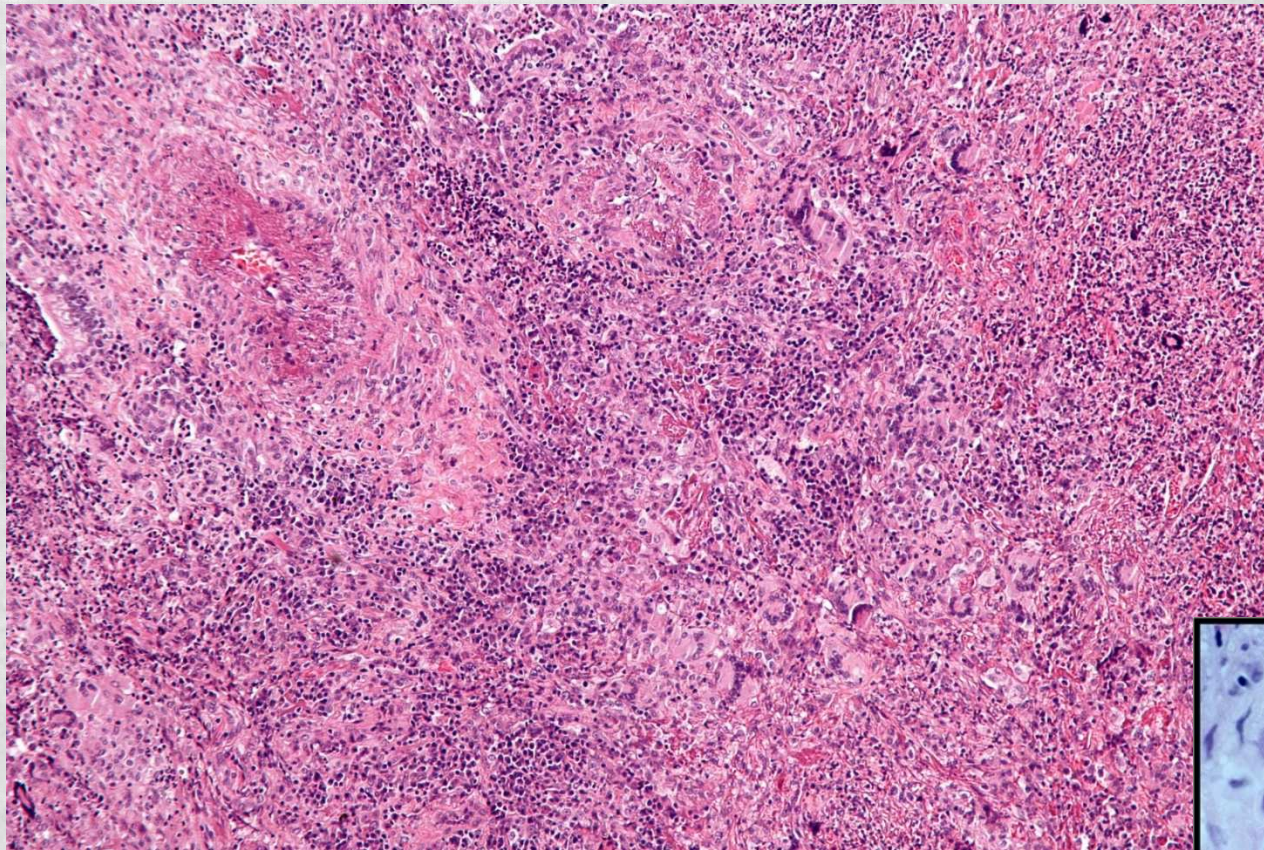


Wegener granulomatosis: palatal destruction

# Wegener Granulomatosis



# Wegener Granulomatosis



**Microscopic polyangitis/ polyarteritis**

## Microscopic polyangitis/ polyarteritis

- It is a systemic small vessel vasculitis associated with glomerulonephritis.
- P-ANCA is characteristically present
- In the past it has been confused with leukocytoclastic vasculitis.

## Churg-Strauss syndrome (additional reading)

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

**Cutaneous leukocytoclastic or hypersensitivity  
vasculitis/ angiitis**

## Cutaneous leukocytoclastic or hypersensitivity vasculitis/ angiitis

- Necrotizing vasculitis of arterioles, capillaries, venules.
- is inflammation of **small blood vessels** (commonly seen in the dermis of skin), characterized by palpable purpura.
- It is the most common vasculitis seen in clinical practice.
- Leukocytoclasia refers to the nuclear debris of infiltrating neutrophils in and around the vessels.
- All lesions tend to be of the same age.
- It affects many organs e.g. skin (most common), mucous membranes, lungs, brain, heart, GI, kidneys and muscle.



# Cutaneous leukocytoclastic or hypersensitivity vasculitis/angiitis

## Causes:

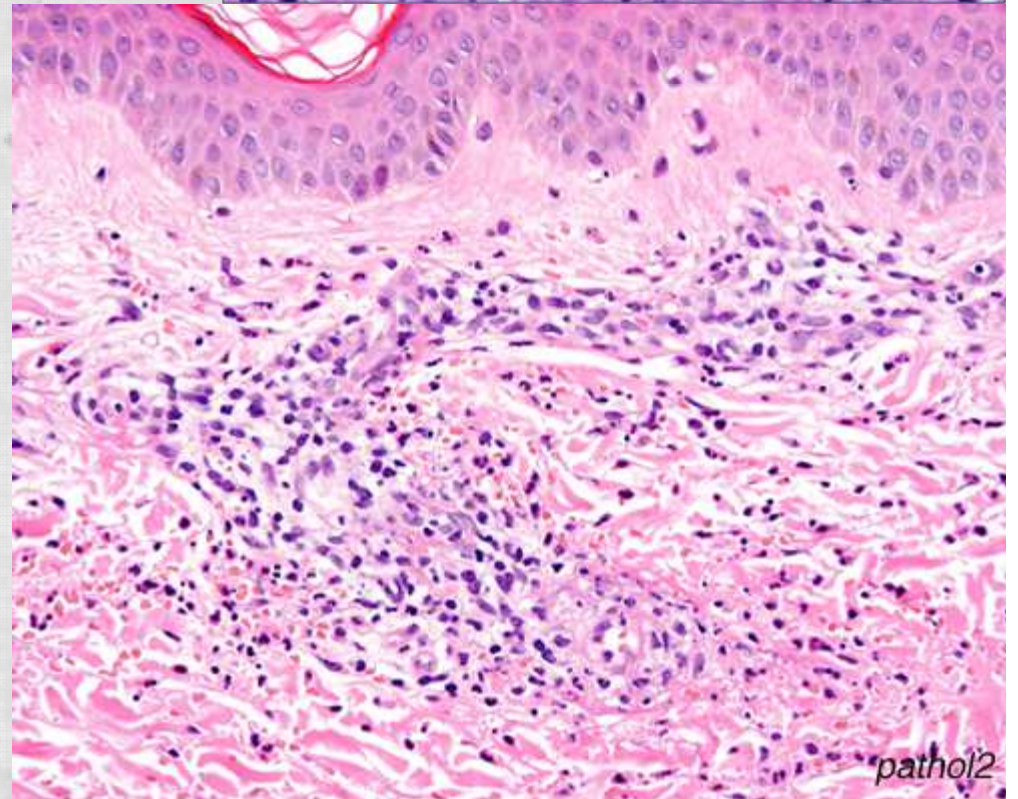
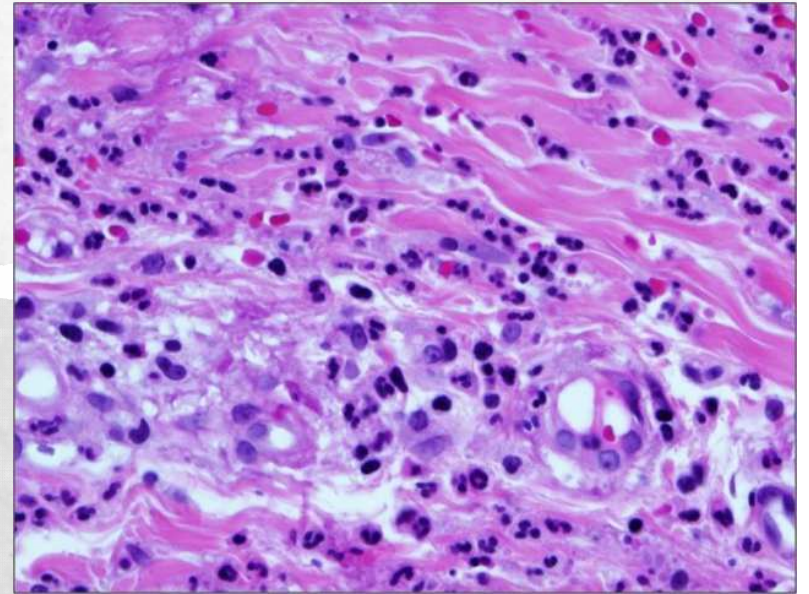
- Idiopathic
- Immunologic reaction to an antigen that may present as
  - Drugs e.g penicillin
  - Infectious microorganisms e.g. strept. and other infections,
  - heterologous proteins,
  - food products and toxic chemicals
  - tumor antigens in various cancers.
- It may be a part of a systemic diseases e.g:
  - **collagen vascular diseases** (lupus erythematosus, rheumatoid arthritis),
  - **Henoch-Schonlein purpura**

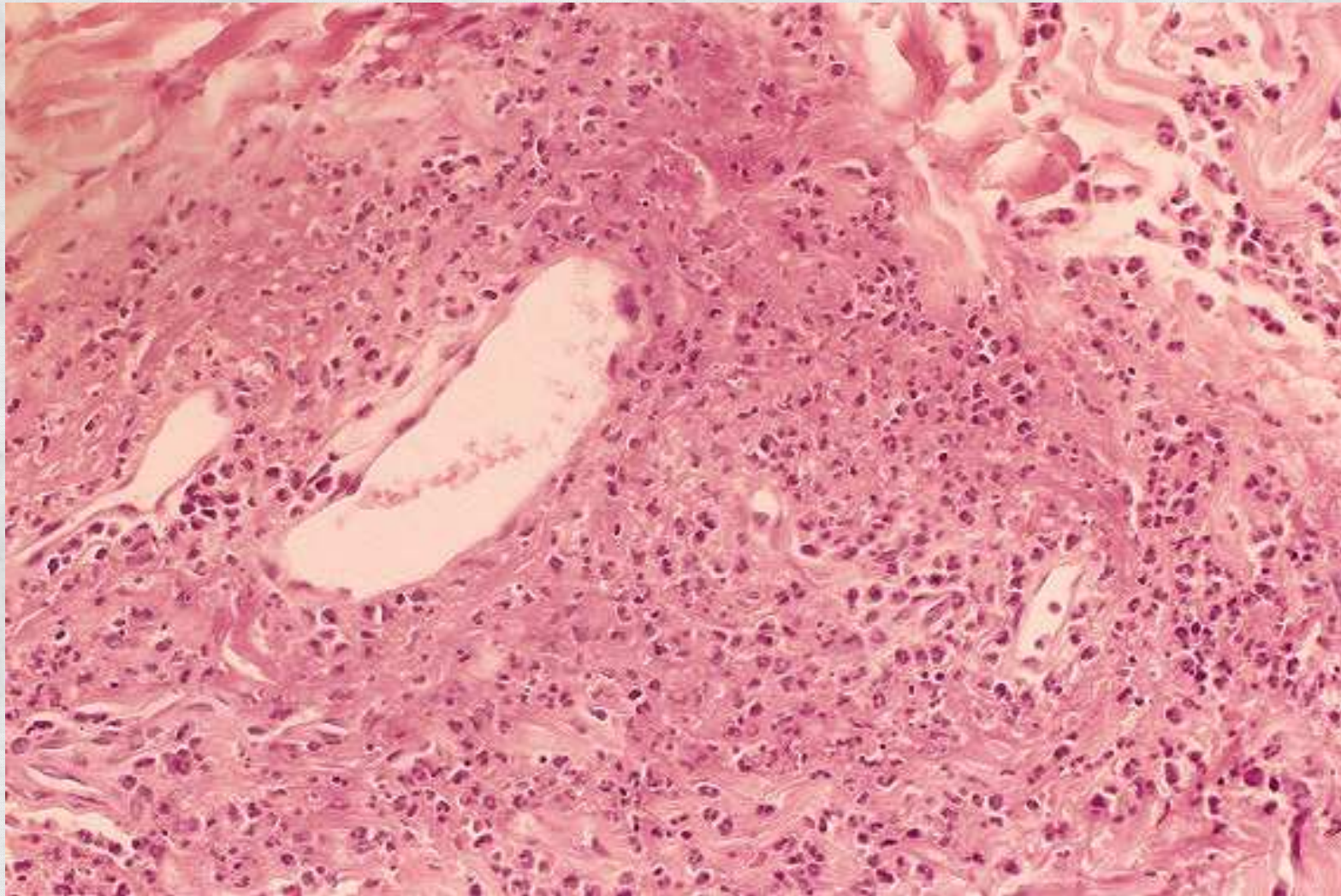
## For home work: Henoch-Schonlein purpura (HSP)

- IgA-mediated, autoimmune systemic disease, in which the small vessels show leukocytoclastic vasculitis.
- The aetiology remains unknown.
- Serum levels of IgA are high in HSP
- Read details from Robbins Pathology

## Cutaneous leukocytoclastic or hypersensitivity vasculitis/ angiitis

- Skin biopsy is often diagnostic.
- Histologically there is infiltration of vessel wall with neutrophils, which become fragmented called as leukocytoclasia or nuclear dust.





Leukocytoclastic vasculitis in a skin biopsy showing fragmentation of neutrophil nuclei in and around vessel walls.

# **Thromboangiitis obliterans (Buerger disease)**

# Thromboangiitis obliterans (Buerger disease)

- It is characterized by segmental, thrombosing, acute and chronic inflammation of medium-sized and small arteries, principally of the leg and hands (tibial and radial arteries), with occasional secondary extension into adjacent veins and nerves.
- Buerger disease is a condition that occurs almost exclusively in heavy smokers of cigarettes, usually beginning before age 35.
- Tobacco either leads to direct toxicity to endothelium, or induces an immune response

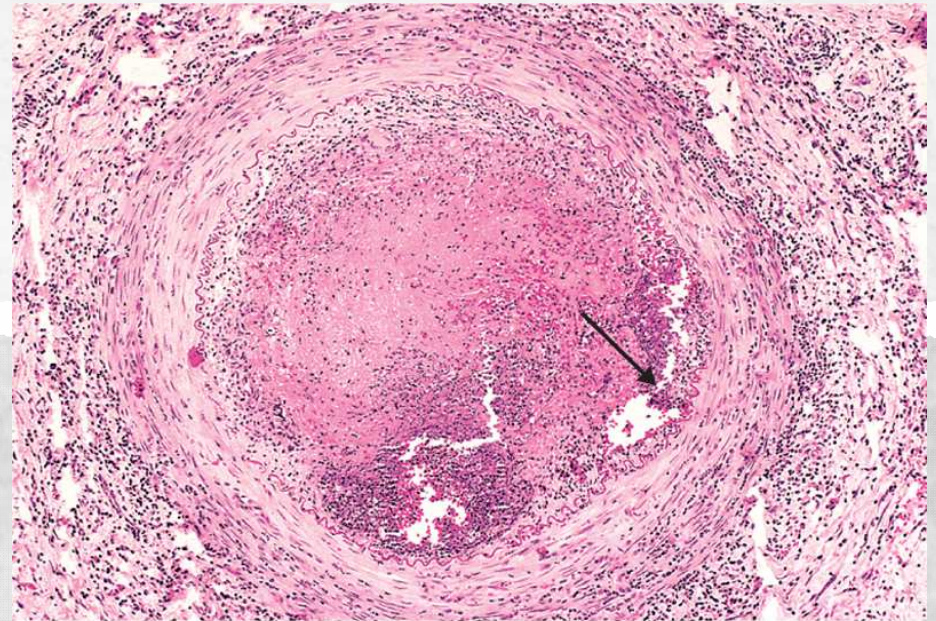


# Thromboangiitis obliterans (Buerger disease)

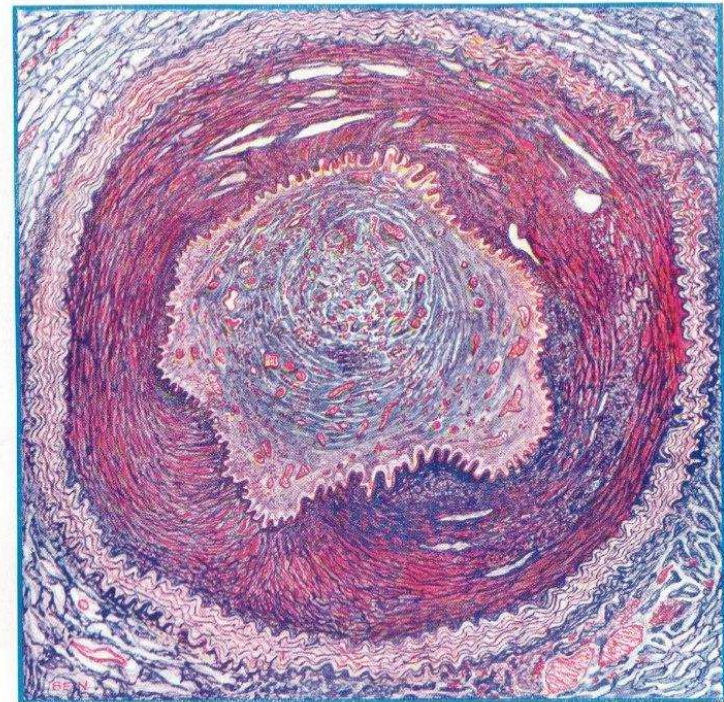
- Clinical features include: pain in the affect hand or foot induced by exercise (called *instep claudication*). Patients can have pain even at rest, due to the neural involvement. Chronic ulcerations of the toes, or fingers may appear, followed in time by gangrene.
- Abstinance from cigarette smoking in the early stages of the disease brings relief from further attacks

## Thromboangiitis obliterans (Buerger disease)

- Microscopically, there is acute and chronic inflammation, accompanied by luminal thrombosis. The inflammatory process extends into adjacent veins and nerves (rare with other forms of vasculitis), and in time all three structures become encased in fibrous tissue.

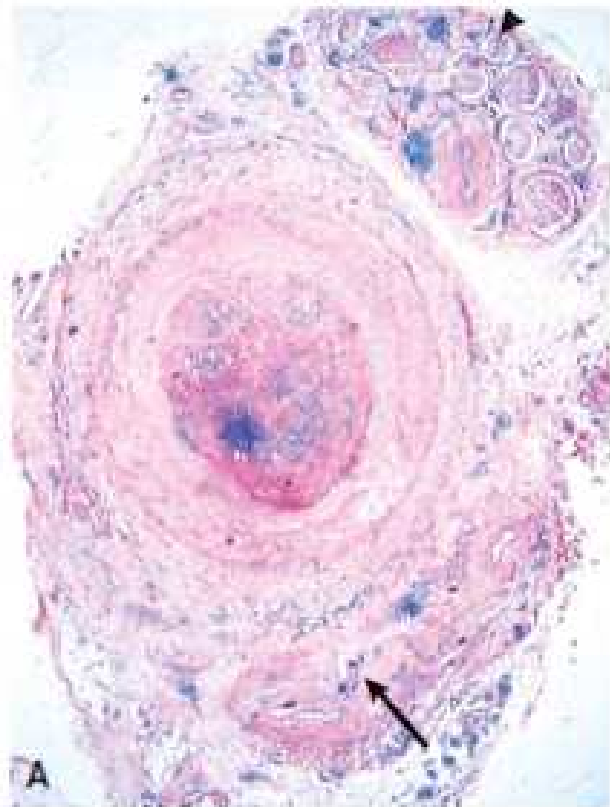


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<https://serendipityproject.files.wordpress.com/2011/09/plate-iii-buergers-disease.jpg>

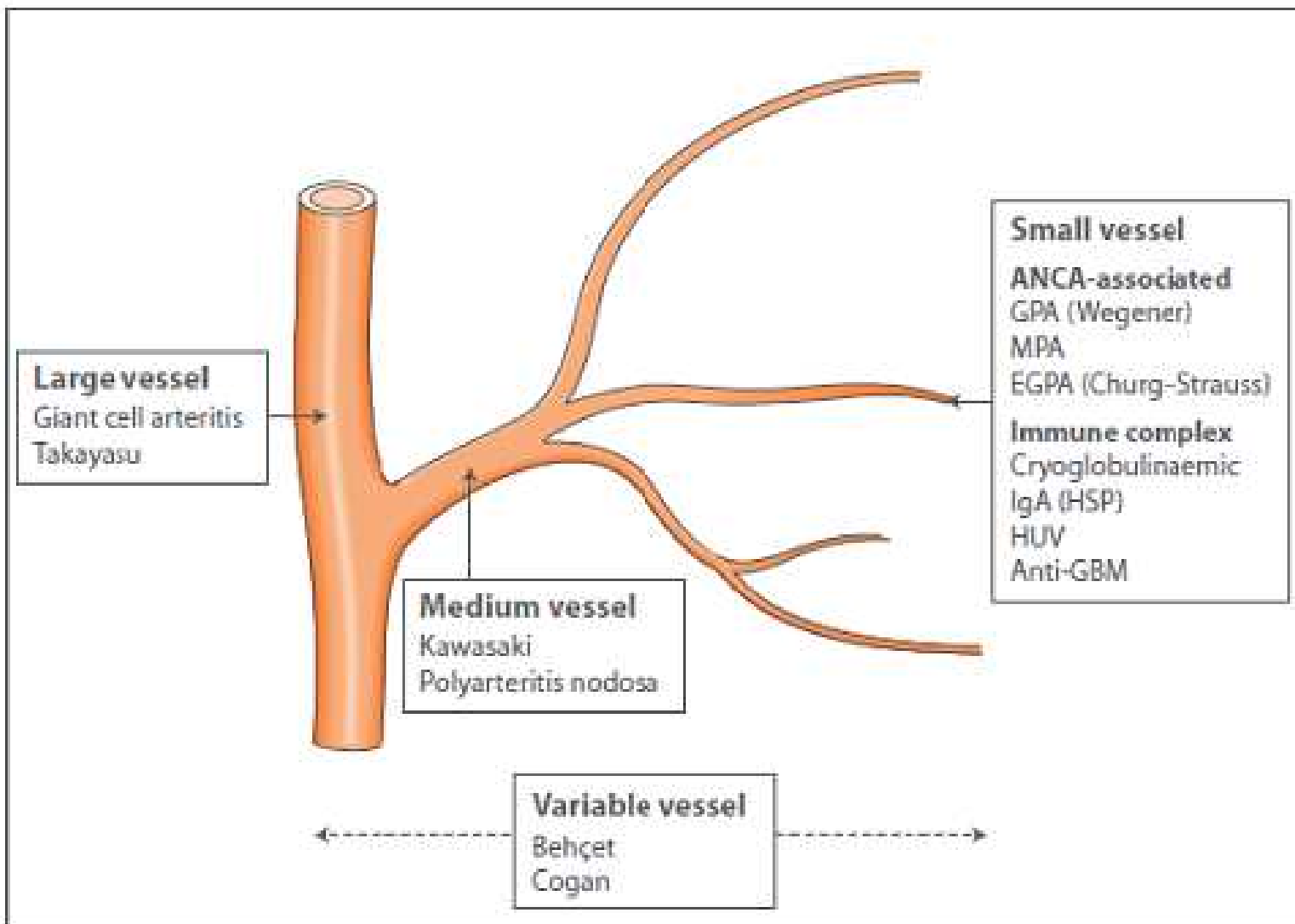




**Buerger disease.** **A.** Section of the upper extremity shows an organized arterial thrombus that has occluded the lumen. Some inflammatory cells are evident in the adventitial fat. In this instance, the vein (*arrow*) and the adjacent nerve (*arrowhead*) show foci of chronic inflammation. **B.** The hand shows necrosis of the tips of the fingers.

## Summary of Vasculitides

Vessel	Disease	comment
Large	Giant-cell arteritis	>50yr. Arteries of head.
	Takayasu arteritis	F <40yr. "Pulseless disease"
Medium	Polyarteritis nodosa	Young adults. Widespread.
	Kawasaki disease	<4yr. Coronary disease. Lymph nodes.
	Berger's disease	35yrs, smokers, extremities
Small	Wegener granulomatosis	Lung, kidney. c-ANCA.
	Churg-Strauss syndrome	Lung. Eosinophils. Asthma. p-ANCA.
	Microscopic polyangiitis	Lung, kidney. p-ANCA.
	Cutaneous leukocytoclastic vasculitis	Idiopathic, infectious, drugs, chemicals, cancer and systemic disease like HNP



**FIGURE 1. Classification scheme for systemic vasculitis.**

ANCA antineutrophil cytoplasmic antibody; EGPA eosinophilic granulomatosis with polyangiitis; GBM glomerular basement membrane; GPA granulomatosis with polyangiitis; HSP Henoch-Schönlein purpura; HUV hypocomplementaemic urticarial vasculitis; IgA immunoglobulin A; MPA microscopic polyangiitis