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:

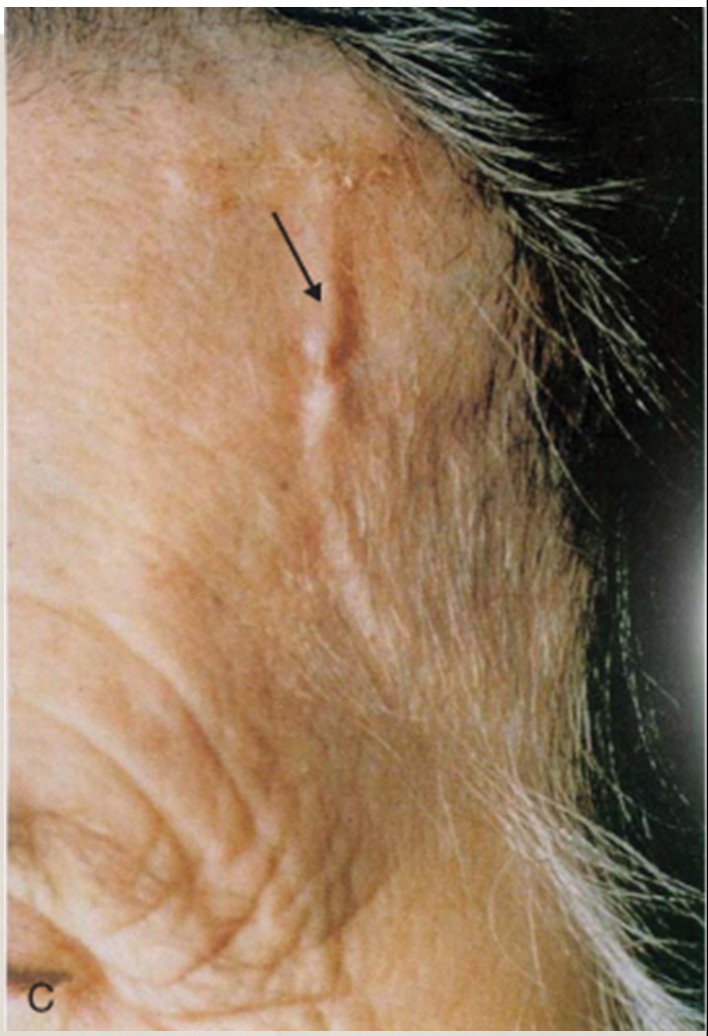
1. Most cases of vasculitis are immune-mediated
   - ❖ Immune complex deposition
   - ❖ Antineutrophil cytoplasmic antibodies (ANCAs)
   - ❖ Anti-endothelial cell antibodies
   - ❖ Autoreactive T cells

2. Vasculitis can also be caused by infection, physical or chemical injury

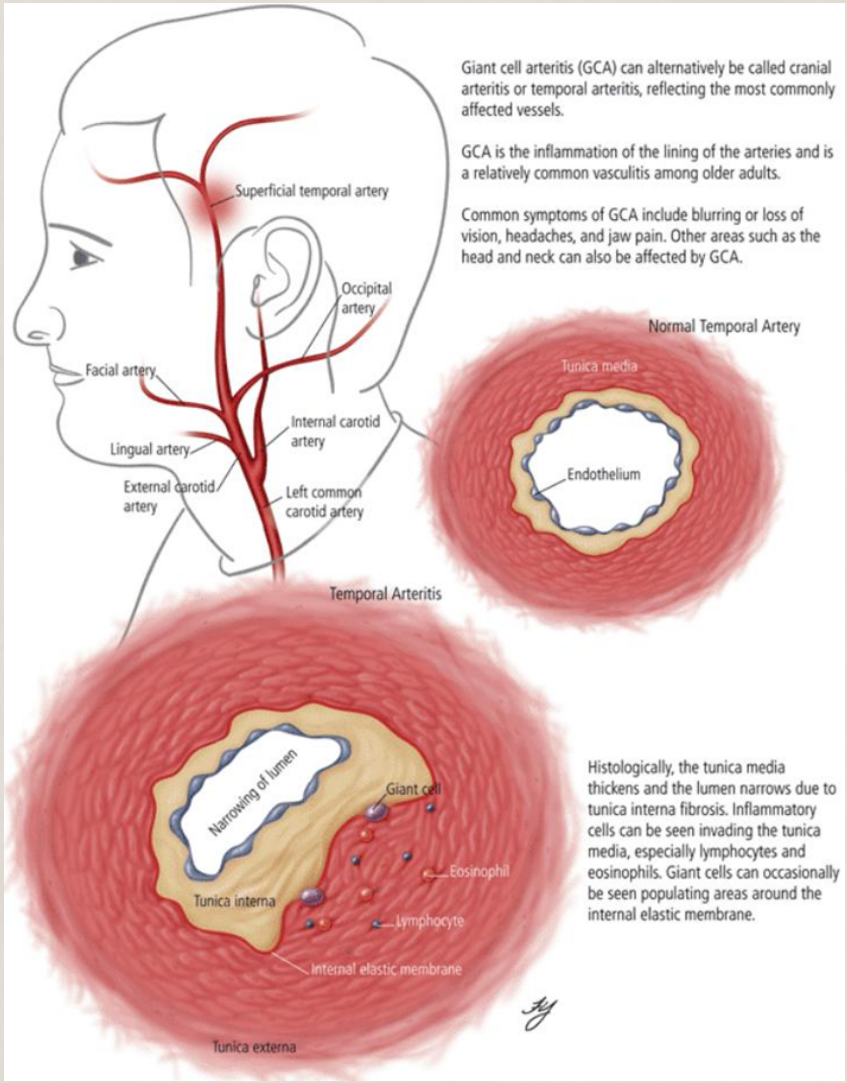
Giant-Cell (Temporal) Arteritis

Giant-Cell (Temporal) Arteritis

- 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)
- Involvment is segmental, acute and chronic.
- It is probably an autoimmune condition.



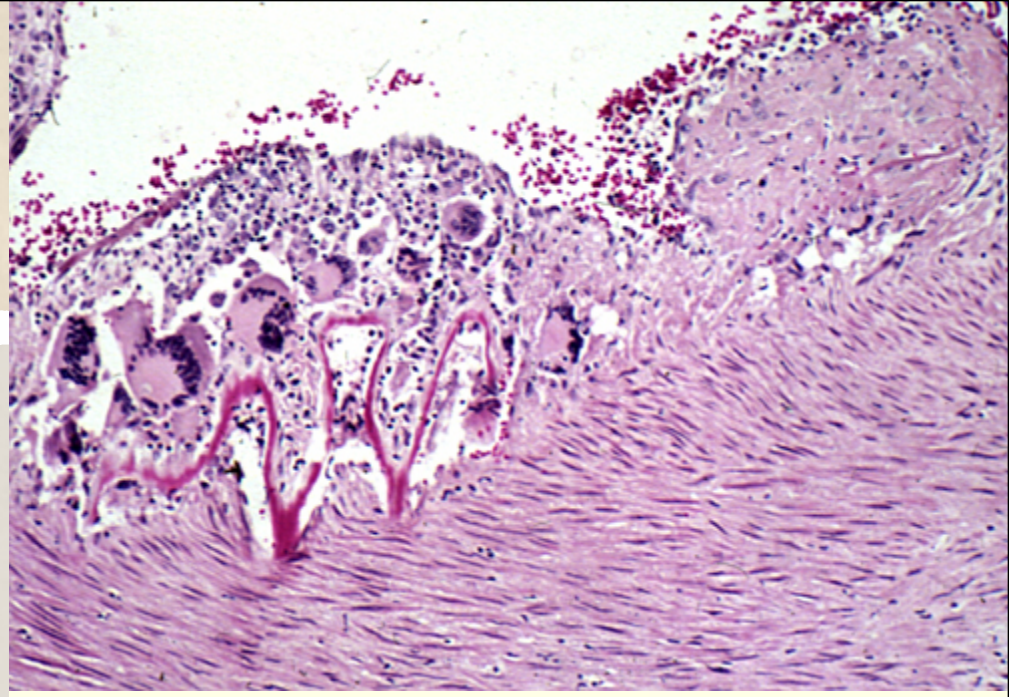
Giant-Cell (Temporal) Arteritis: Clinical Features



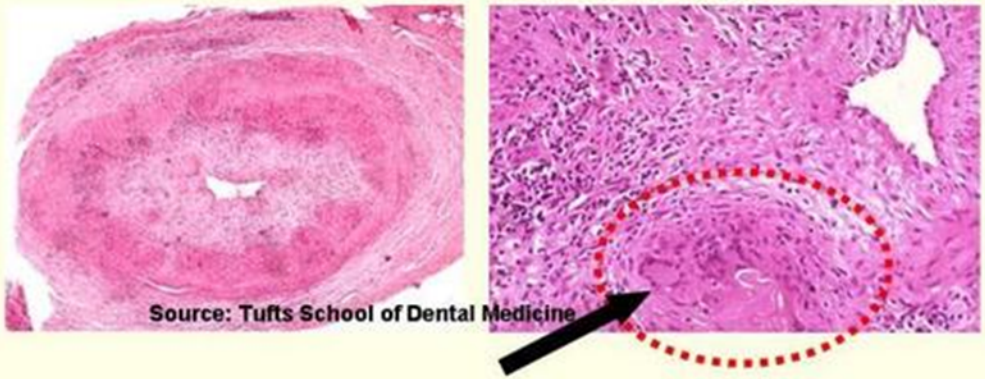
- Symptoms :
  - ✓ fever, facial pain or headache, often most intense along the course of the superficial temporal artery,
  - ✓ Thickened and painful temporal artery
  - ✓ Jaw pain
  - ✓ Visual problems and acute vision loss
- The diagnosis depends on biopsy and histologic confirmation.
- Treatment: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

Biopsy of 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

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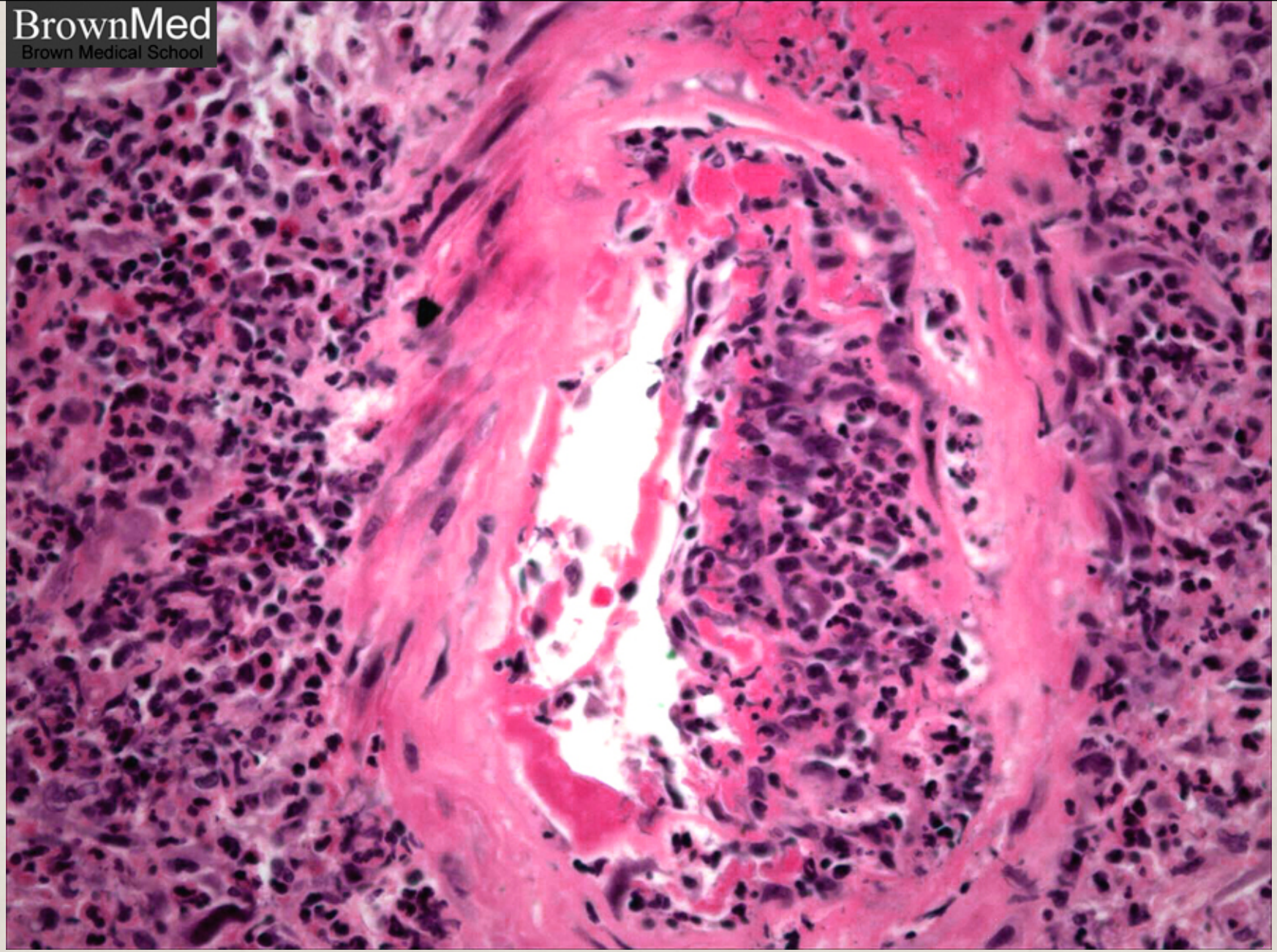
Polyarteritis Nodosa

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

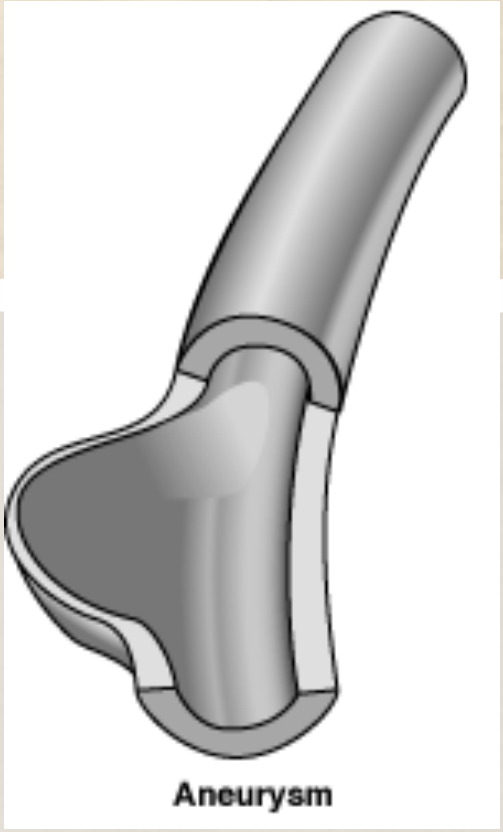
- Some clinical manifestations are due to ischemia and infarction of affected tissues/ organs.
- Fever, weight loss, abdominal pain and melena (bloody stool), muscular pain and neuritis.



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.



Granulomatosis with Polyangiitis (also known as Wegener granulomatosis)

Granulomatosis with Polyangiitis (also known as Wegener granulomatosis)

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

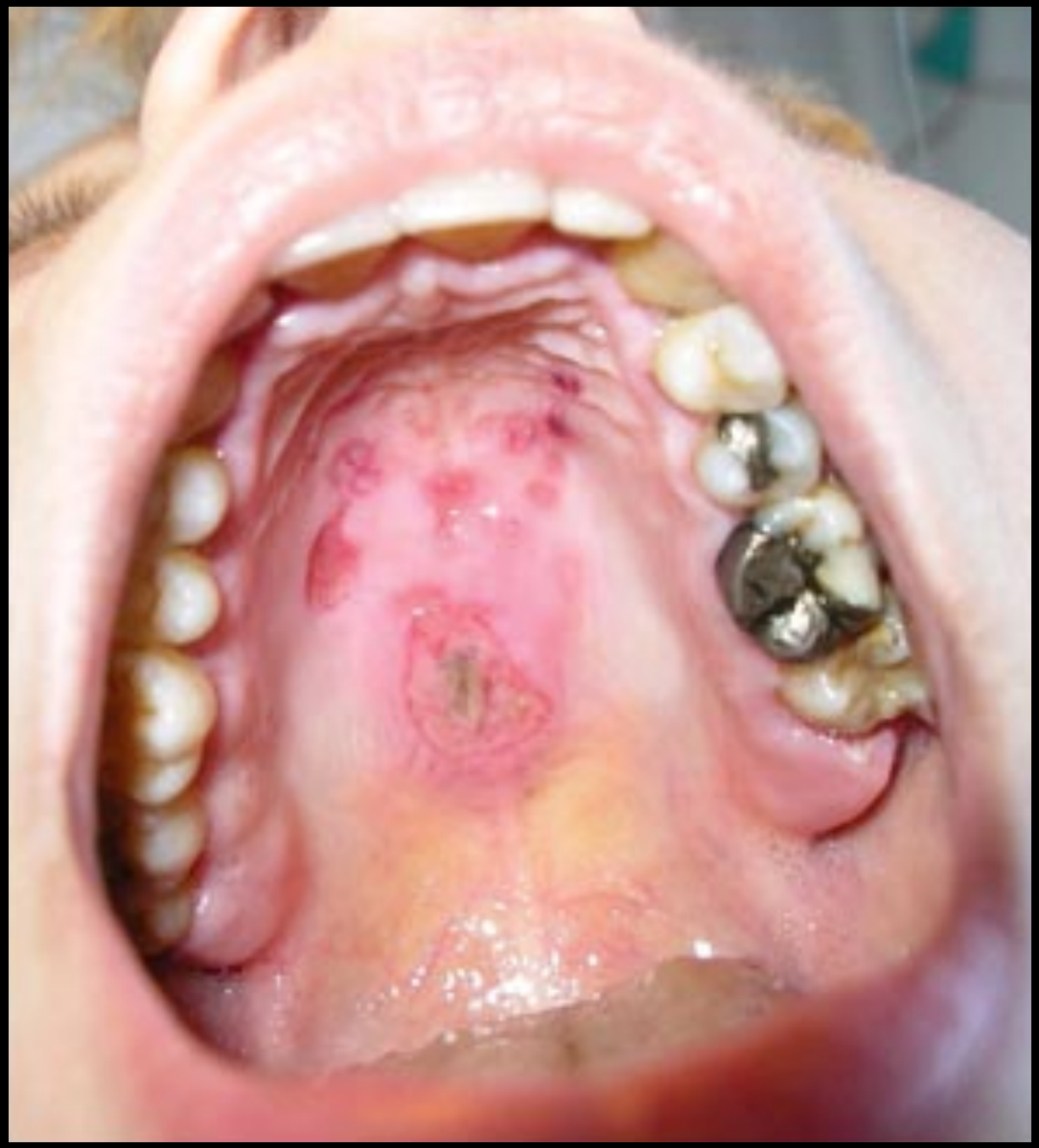
1) **necrotizing granulomas** of the upper and lower respiratory tract

2) necrotizing or granulomatous **vasculitis** of small to medium-sized vessels

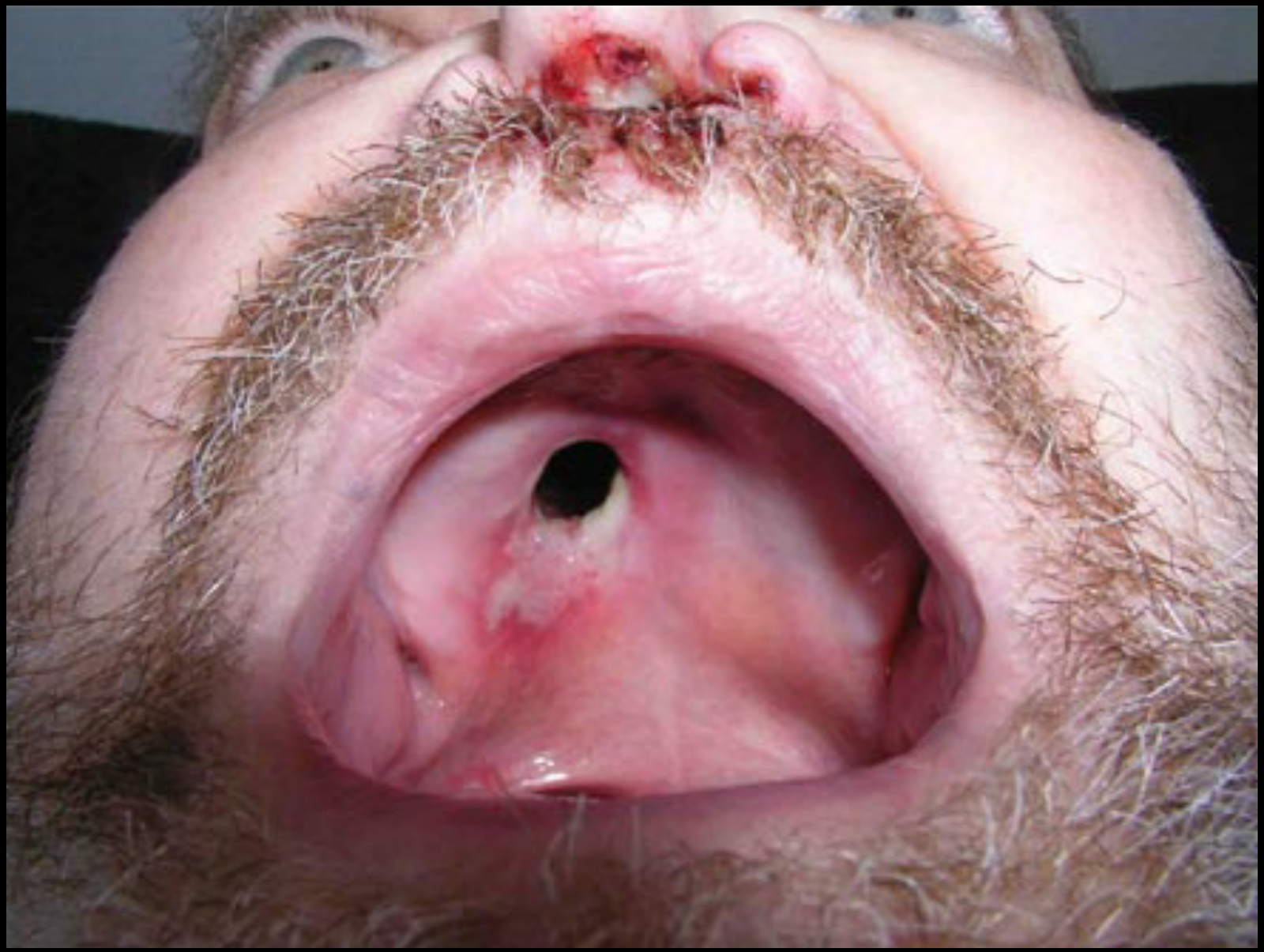
3) **renal disease** in the form of necrotizing, crescentic, glomerulonephritis.

Granulomatosis with Polyangiitis (also known as Wegener granulomatosis)

- Males are affected more often than females, at an average age of about 40 years
- **C-ANCAs (**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.

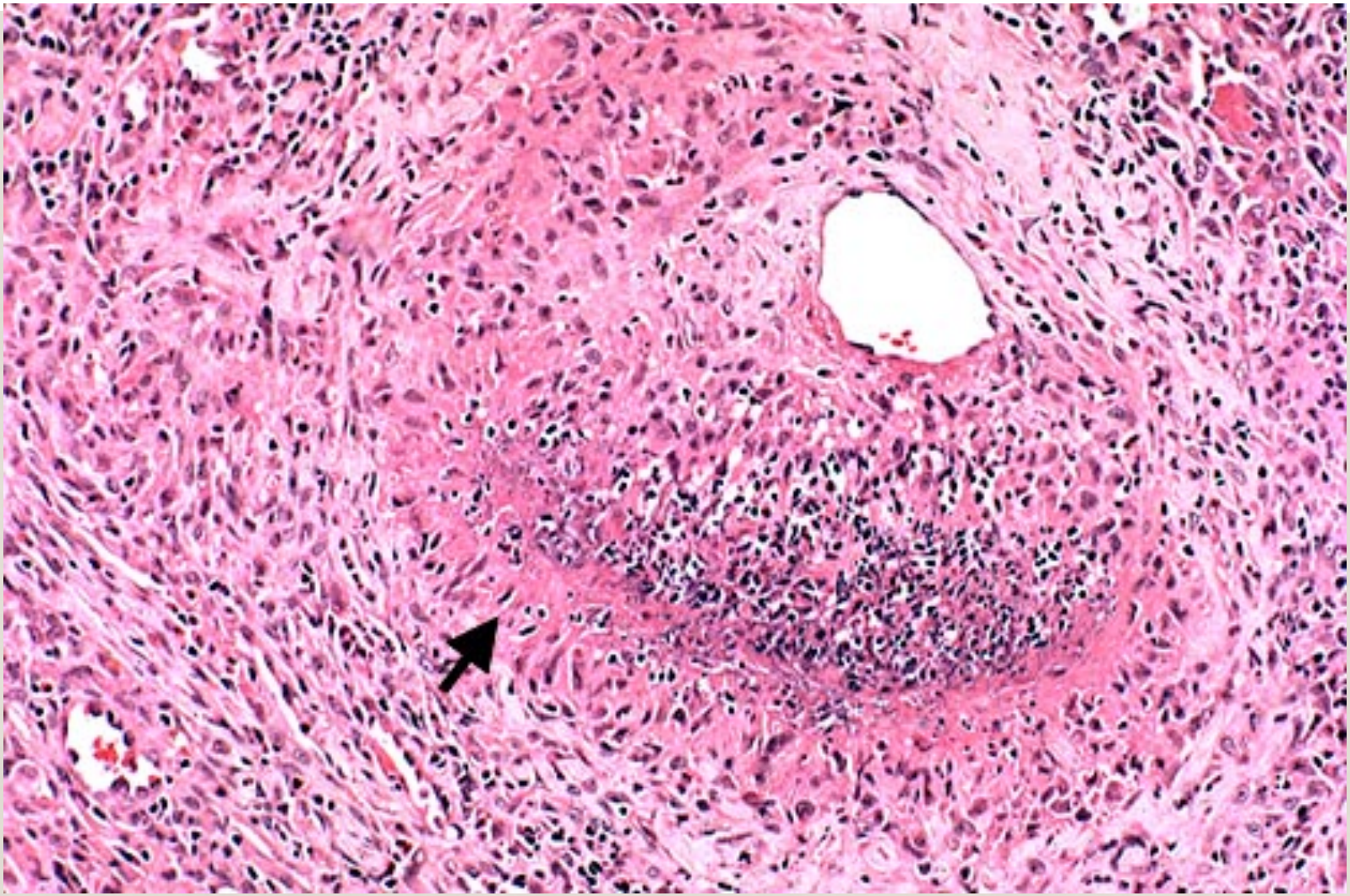


Wegener granulomatosis: palatal ulceration

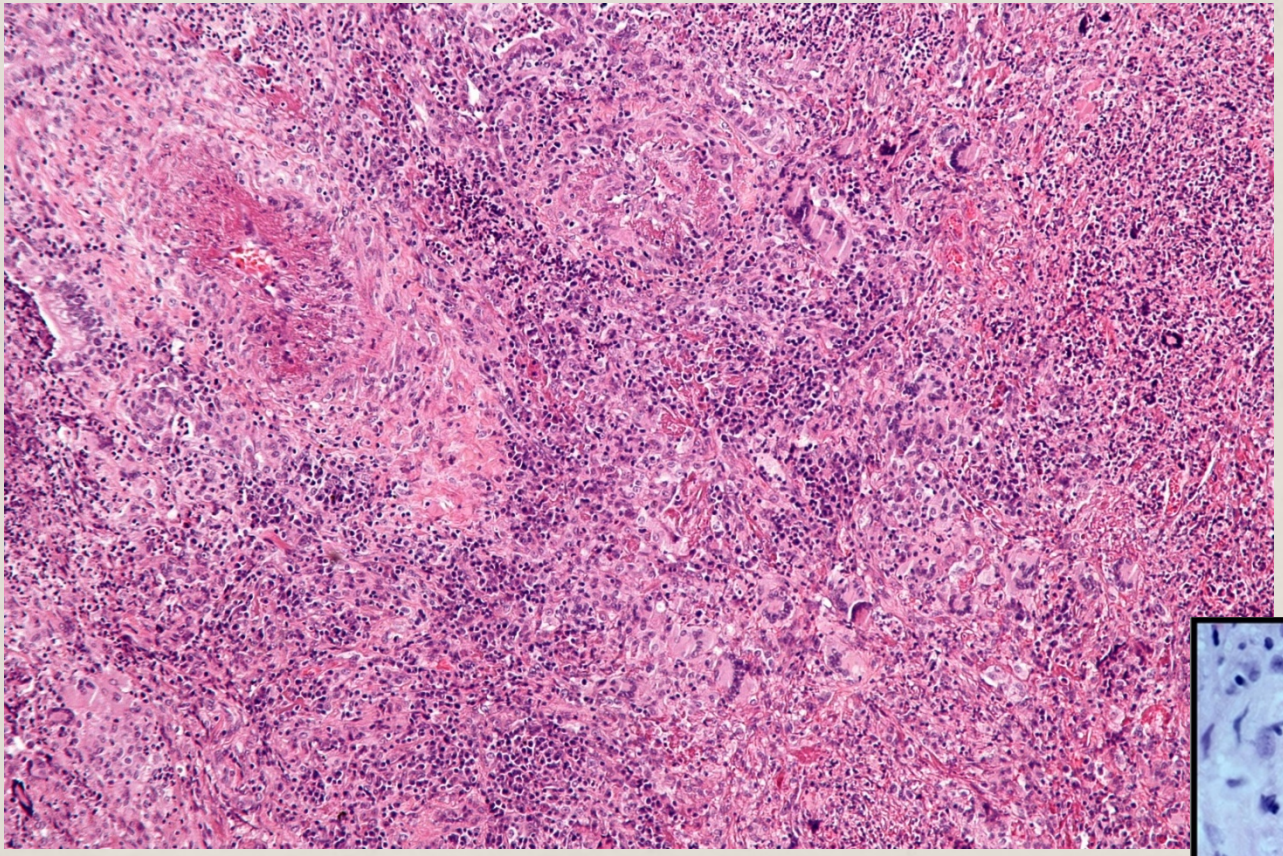


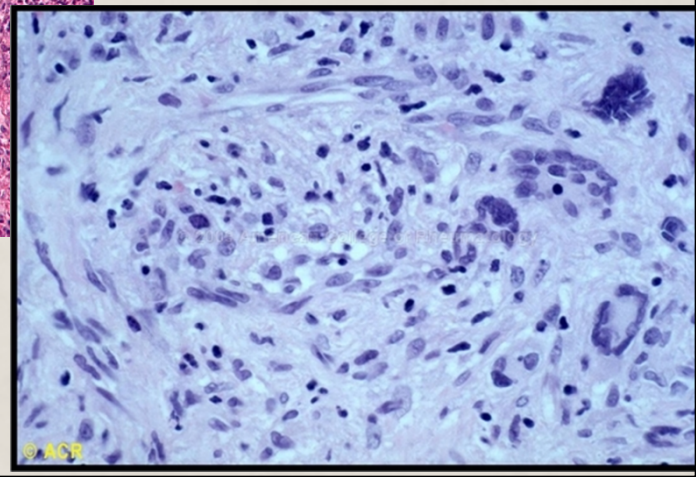
Wegener granulomatosis: palatal destruction

Granulomatosis with Polyangiitis (also known as Wegener granulomatosis)



Granulomatosis with Polyangiitis (also known as Wegener granulomatosis)





Microscopic polyangitis/ polyarteritis

Microscopic polyangitis/ polyarteritis

- It is a systemic small vessel vasculitis associated with glomerulonephritis (renal disease).
- **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-ANCAs.

Cutaneous leukocytoclastic (hypersensitivity vasculitis/ angiitis)

Cutaneous leukocytoclastic (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.
- Leukocytoclasis 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 (hypersensitivity vasculitis/angiitis)

Causes:

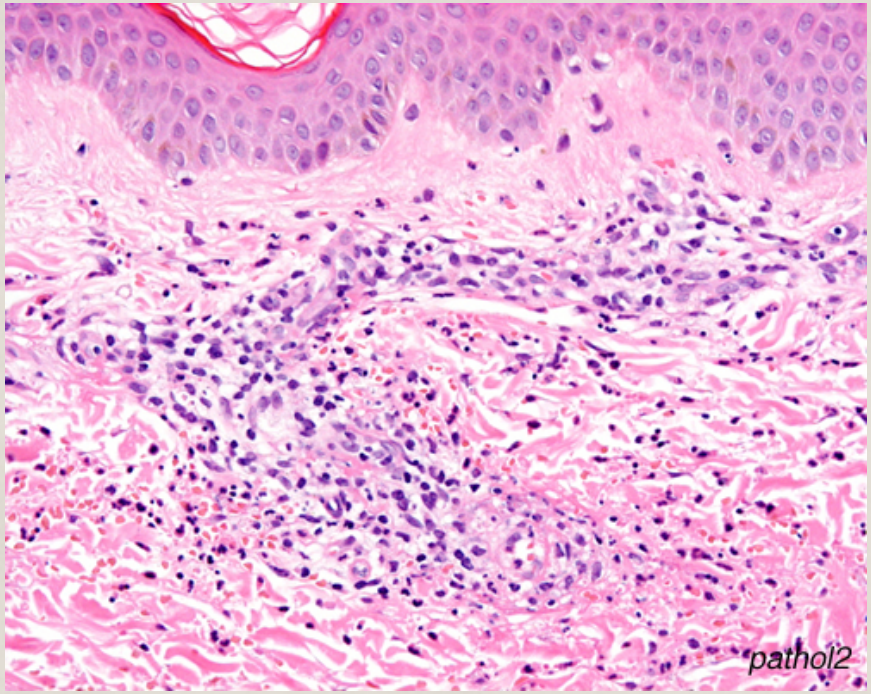
- Idiopathic
- Immunologic reaction to an antigen that may present as
  - Drugs e.g. penicillin
  - Infectious microrganisms e.g. strept. and other infections,
  - heterologous proteins,
  - food products and toxic chemicals
  - tumor antigens in various cancers.
- It may be a part of a systemic diseases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

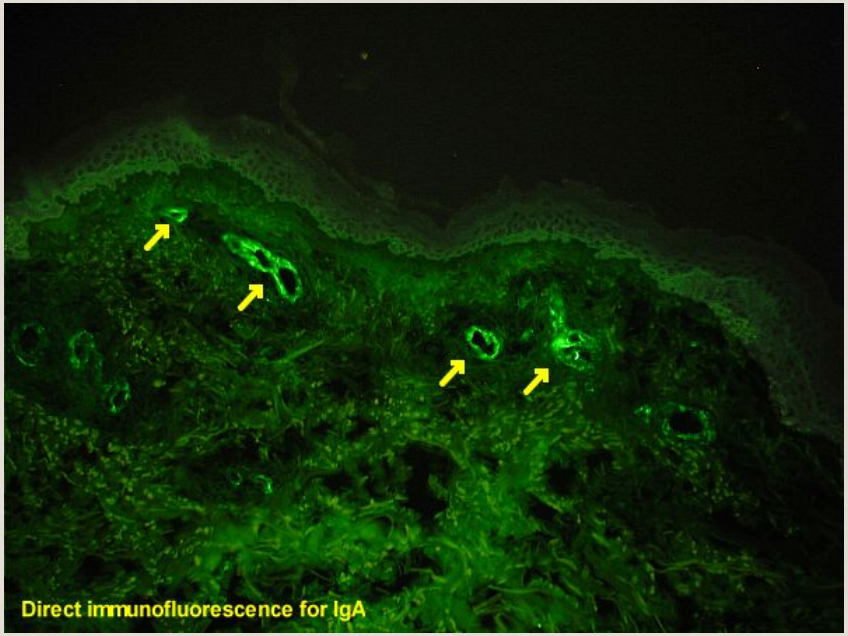
Henoch-Schonlein purpura (HSP)

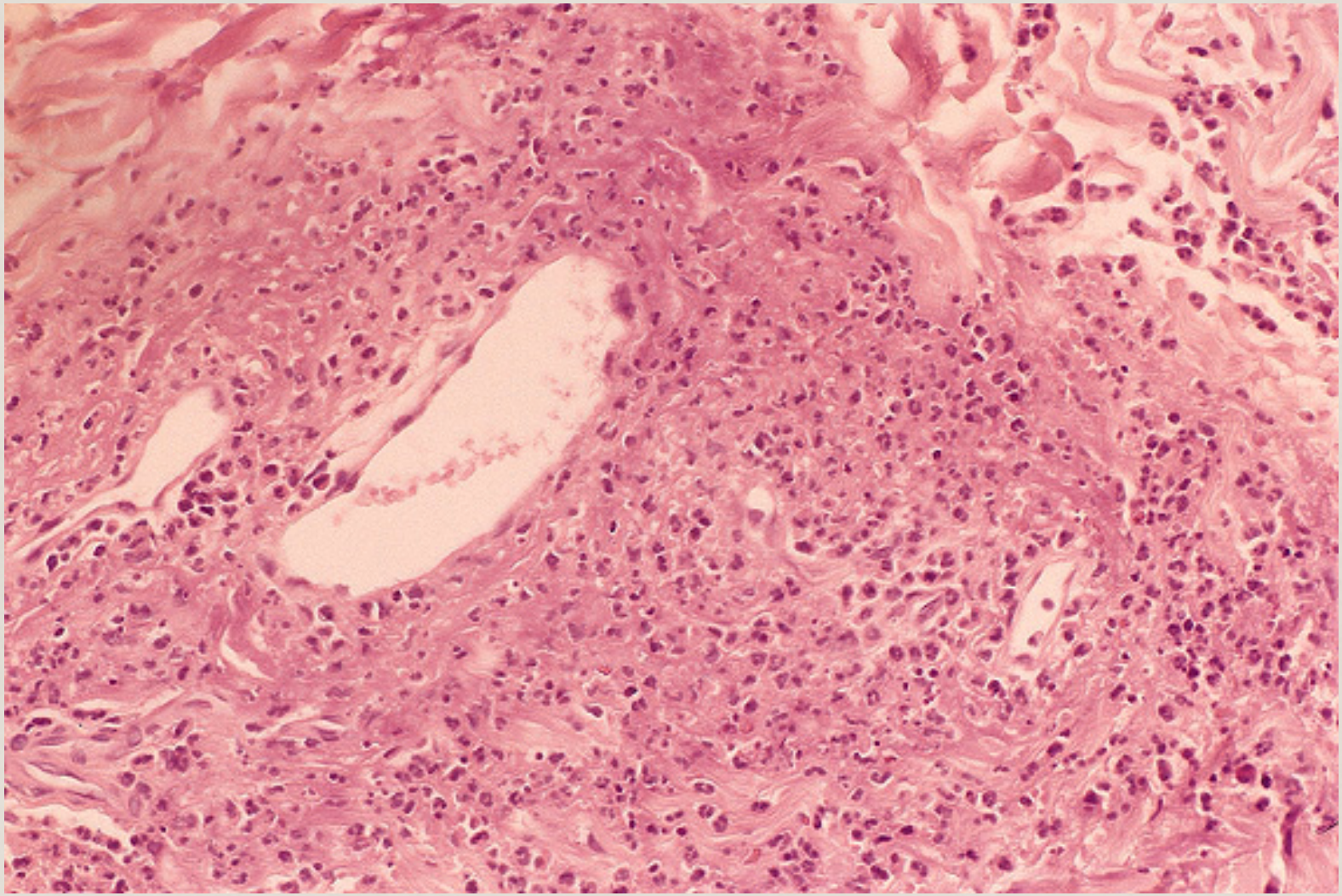
- HSP is an IgA-mediated, autoimmune systemic disease in which the small vessels show leukocytoclastic vasculitis.
- The etiology remains unknown.
- Serum levels of IgA are high in HSP
- Skin biopsy will show necrotizing leukocytoclastic vasculitis of capillaries in the dermis.
- The immunofluorescence shows IgA immunoglobulin deposition in the wall the affected capillaries.

Cutaneous leukocytoclastic (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.
- The direct *immunofluorescence will show* deposits of IGA immunoglobulin in the wall the capillaries in **Henoch-Schonlein purpura (HSP) .**





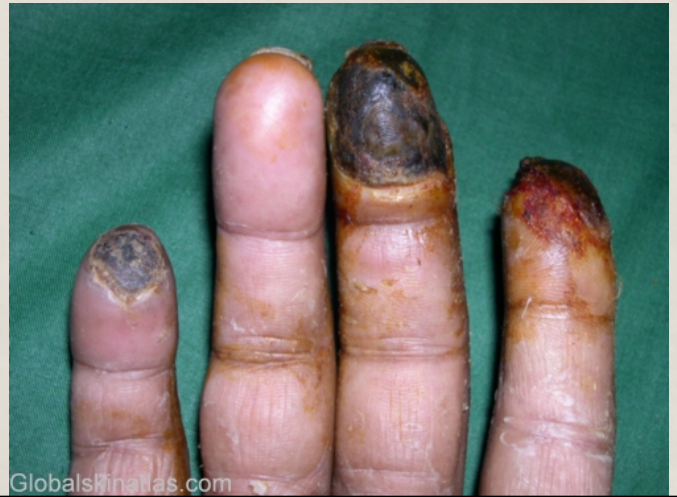


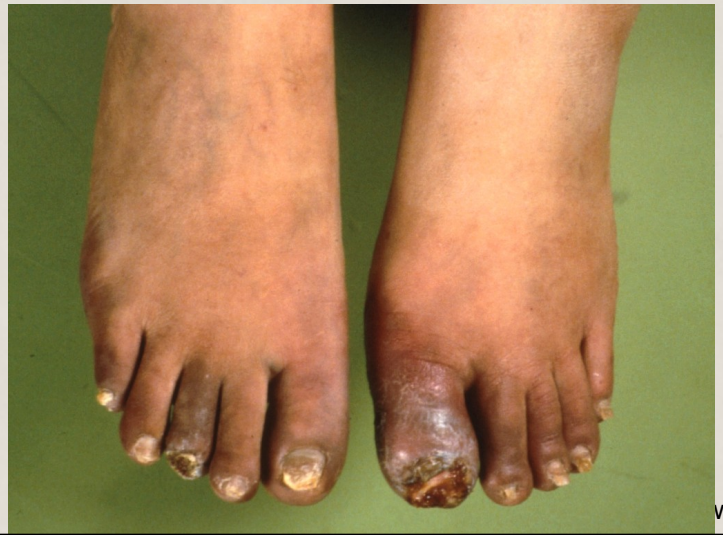
Leukocytoclastic vasculitis in a skin biopsy showing fragmentation of neutrophil nuclei in and around vessel walls.

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 **secondary extension into adjacent veins and nerves**.
- Buerger disease is a condition that occurs almost exclusively in heavy smokers of cigarettes
- Patients are usually under 35 years of age.
- Tobacco either leads to direct toxicity to endothelium, or induces an immune response



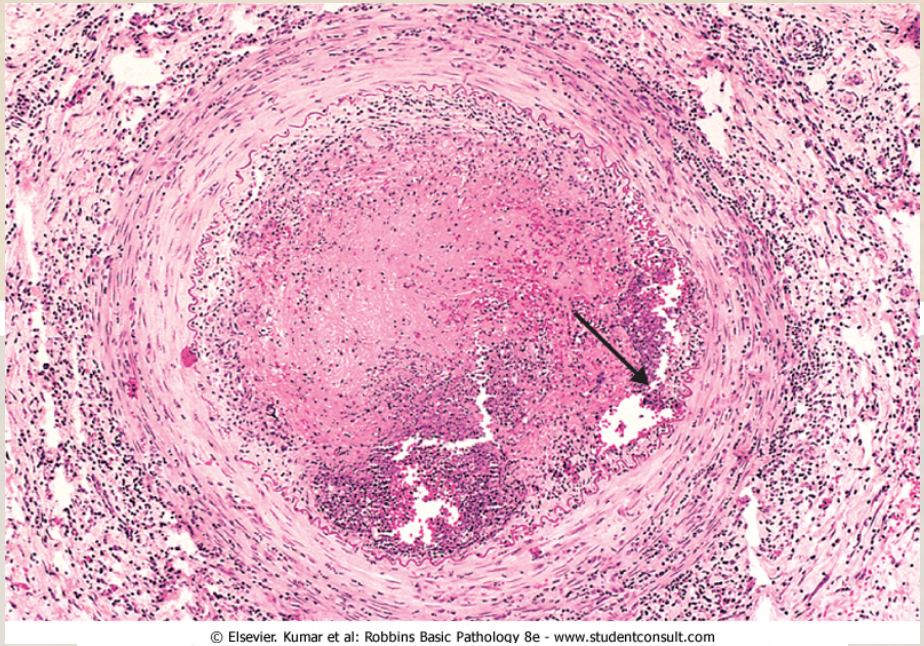


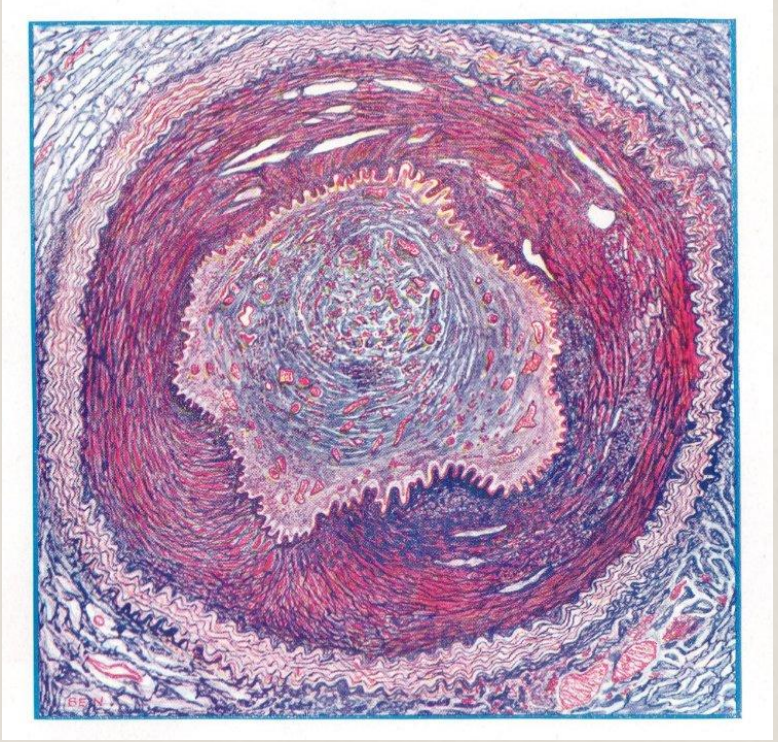
Thromboangiitis obliterans (Buerger disease)

- Clinical features include: pain in the affected 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.
- Abstinence 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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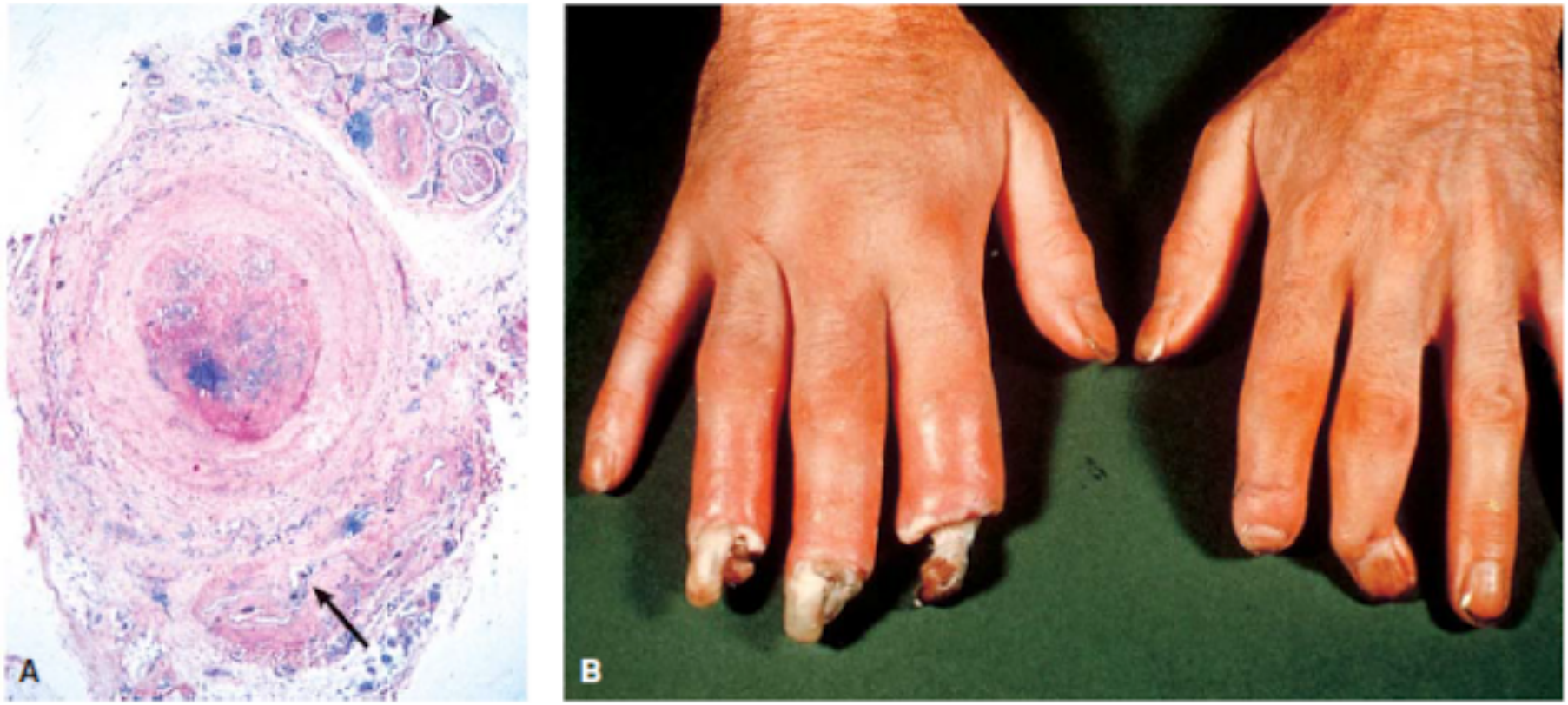

Buerger disease. A. Section of the upper extremity shows an organized arterial thrombus that has occluded the lumen. Some inflammatory cells are evident in the adventitial fat. In this instance, the vein (*arrow*) and the adjacent nerve (*arrowhead*) show foci of chronic inflammation. **B.** The hand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

http://4.bp.blogspot.com/-bZxbAr2dKw0/VcC6qksT8kI/AAAAAAAABes/xvvUOdWiIxM/s640/Buerger%2BDisease.PNG

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

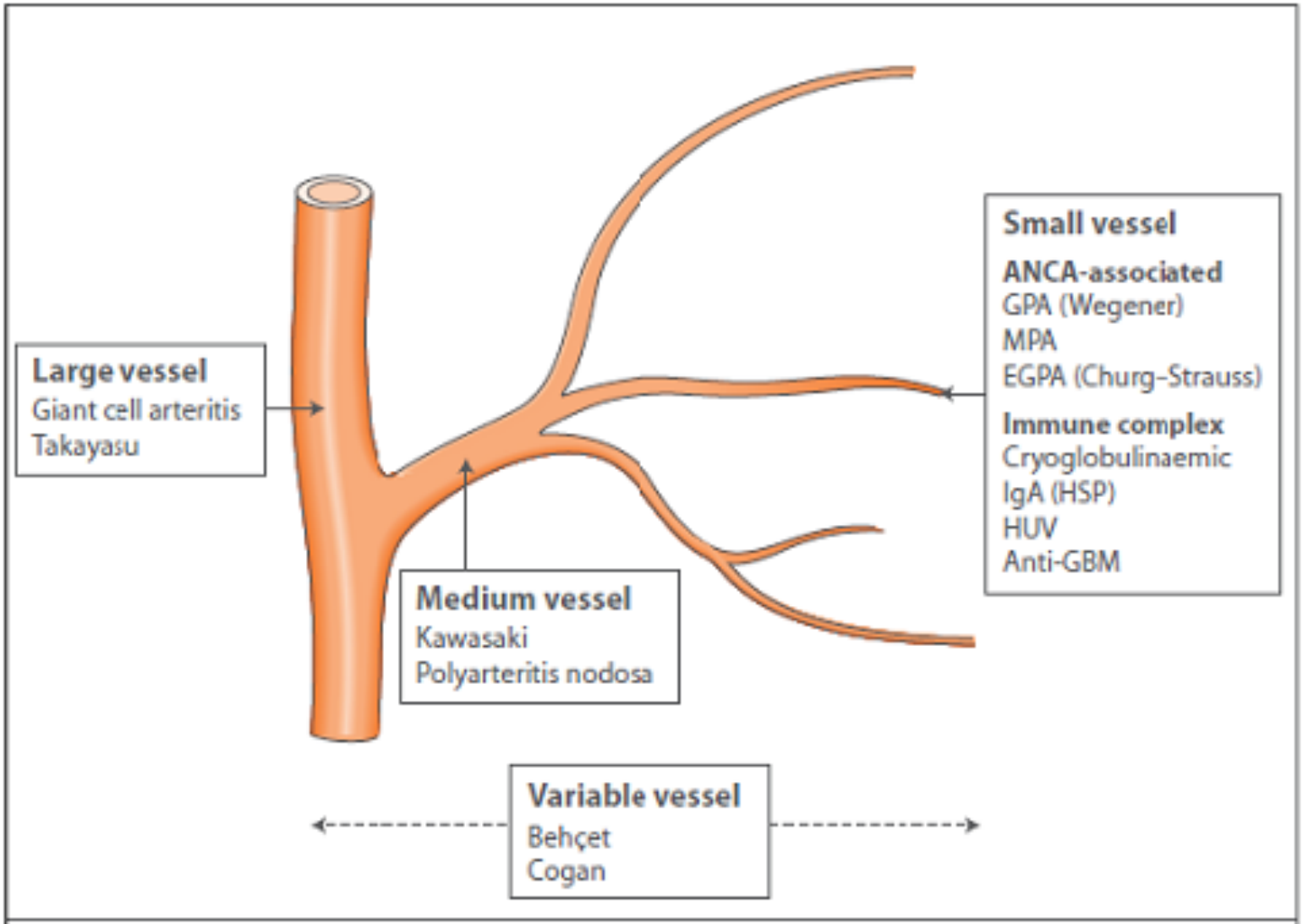

FIGURE 1. Classification scheme for systemic vasculitis.

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

http://www.arthritisresearchuk.org/~/media/Images/Educational-resources/Reports%20images/TR_7_1/TR_7_1_fig1.ashx?la=en

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