Vasculitis

- Inflammation of the vessel wall.
- Signs and symptoms:

1- **local:** according to the involved tissue

2- **systemic**:(fever, myalgia, arthralgias, and malaise)

Pathogenesis

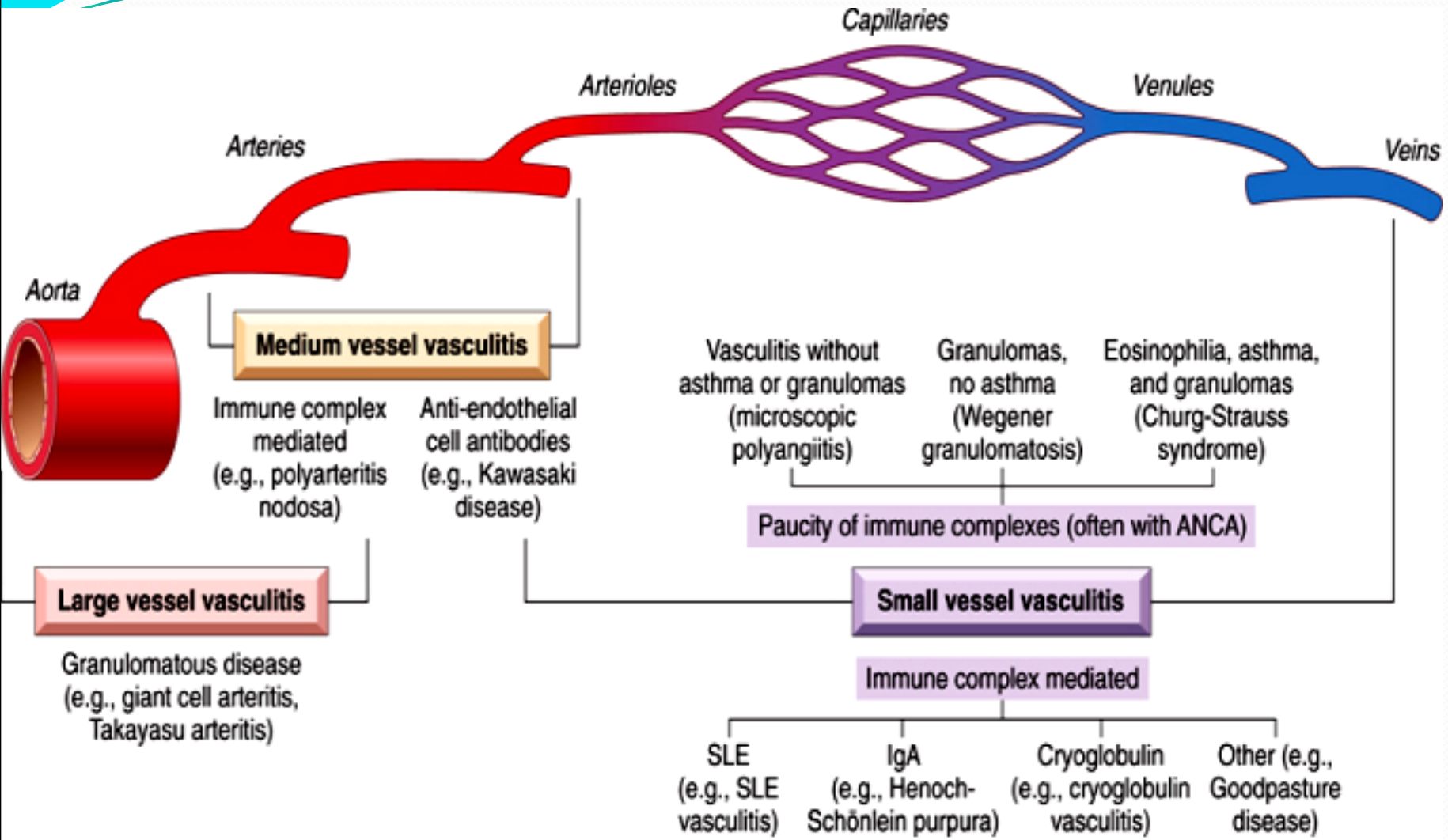
1- immune-mediated inflammation

2- infectious pathogens.

- It is critical to distinguish between infectious and immunologic mechanisms due to the huge difference in management.

3- Physical injury (radiation, mechanical trauma)

4- chemical injury (toxins)



Kumar et al: Robbins Basic Pathology, 9e.

- ***immunologic mechanisms*** **of vasculitis :**

1- **Immune complex** deposition

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

3- **Anti-endothelial cell antibodies**

4- **Auto-reactive T cells**

1- Immune complex deposition

Example: ***<u>Drug</u> hypersensitivity vasculitis***.

- e.g., penicillin
- vary from mild and self-limiting, to severe and even fatal
- skin lesions are most common.
- Treatment: discontinuation of the offending drug.

2- Anti-Neutrophil Cytoplasmic Antibodies (ANCA)

- **ANCAs** = circulating antibodies that react with neutrophil cytoplasmic antigens

- ANCAs blood levels are very useful markers for diagnosis, severity, and predictive of disease recurrence.

- two types are most important:

1-Antiproteinase-3 (PR3-ANCA)

= **c-ANCA**.

- azurophilic granule constituent
- e.g. Wegener granulomatosis

2-Anti-myeloperoxidase (MPO-ANCA)

p-ANCA.

- lysosomal granule constituent
- e.g. Churg-Strauss syndrome

3- Anti-Endothelial Cell Antibodies

- Antibodies against endothelial cells
- Associated with Kawasaki disease (discussed later).

Types of vasculitis

1- Giant Cell (Temporal) Arteritis

- ***most common vasculitis in elderly in developed countries.***
- *chronic* ***granulomatous*** *inflammation of large arteries*
- ***temporal*** *arteries;* *v*ertebral; ophthalmic; aorta also can be involved.
- ***Pathogenesis*****: T cell-mediated immune response**
- ***Morphology*****:**
- **granuloma (75%) → inner media and internal elastic membrane**
- **fragmentation of internal elastic lamina**

Giant Cell (Temporal) Arteritis

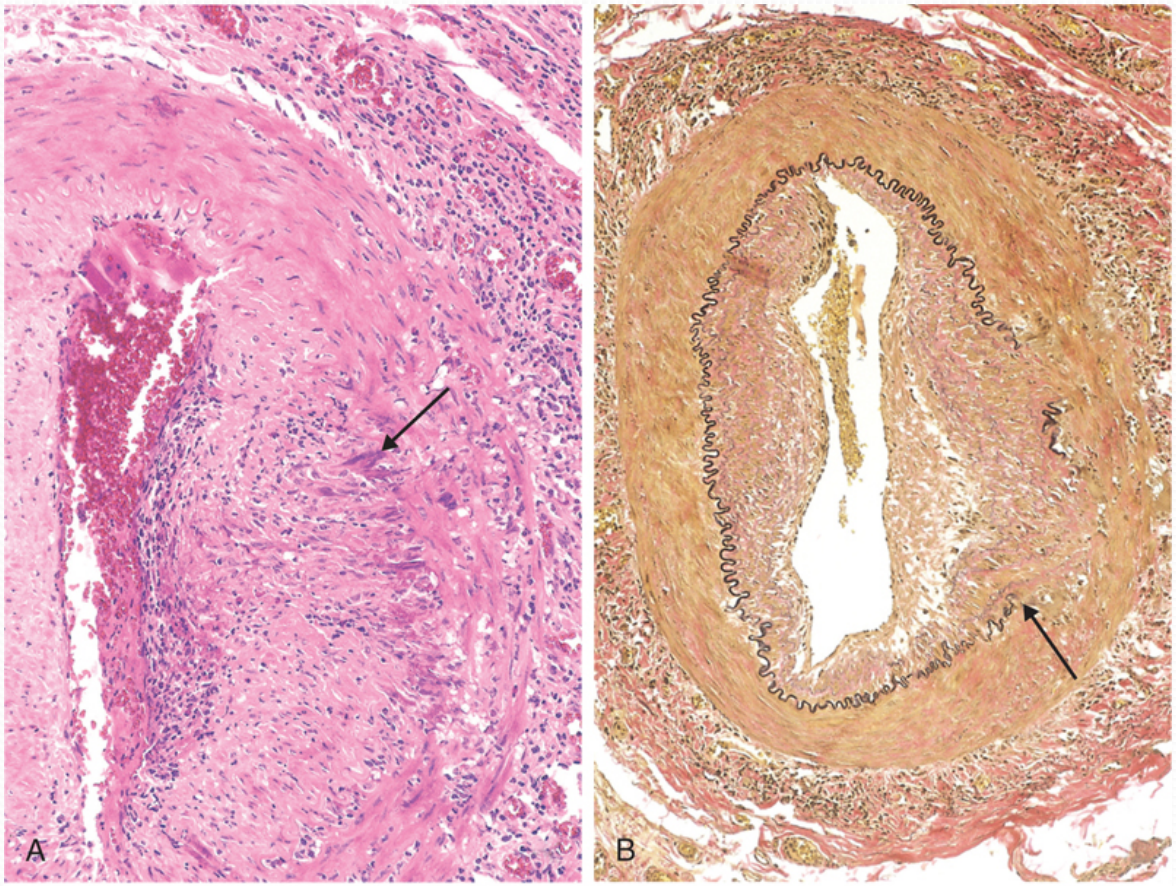
- **rare before age 50.**
- ***Signs and symptoms:***
- **fever, fatigue, weight loss**
- **facial pain, headache (superficial temporal artery).**
- **Ocular symptoms (ophthalmic artery); diplopia to complete vision loss** (rapid diagnosis and treatment are mandatory).
- ***Diagnosis*:**

- Vessel biopsy and histology

- ***Treatment*:**

- Corticosteroid or anti-TNF therapies

(Giant Cell (Temporal) Arteritis morphology (arrows) A> granuloma; B> fragmented internal elastic lamina



2- Takayasu Arteritis

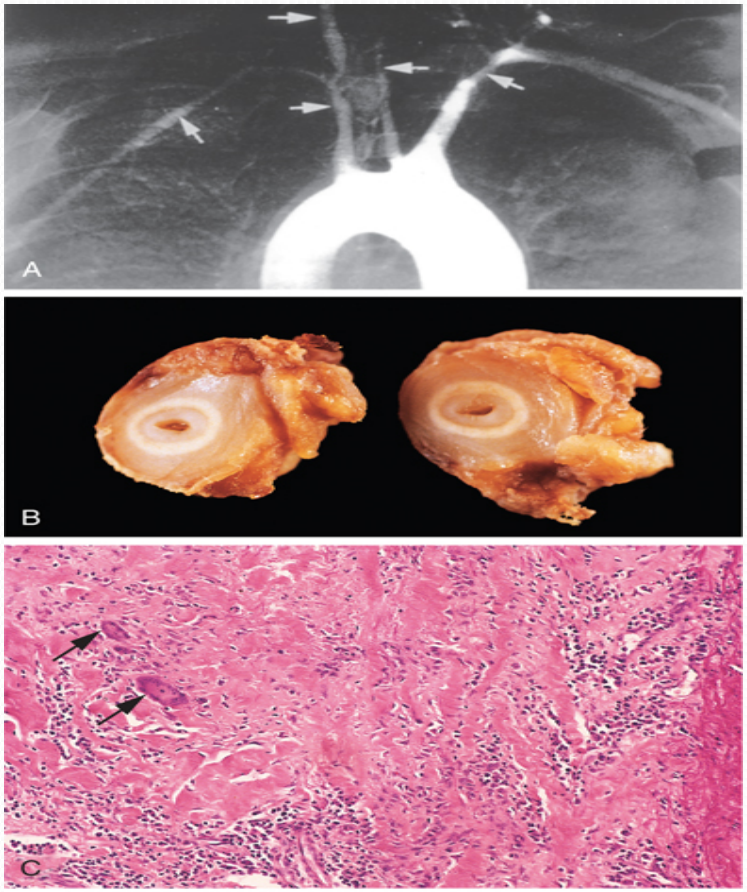
- vasculitis of large and medium-sized arteries
- *aortic arch and arch vessels* (2/3) →scarring and thickening with severe luminal narrowing of major branch vessels.
- marked weakening of pulses in upper extremities (= the pulseless disease).

Takayasu arteritis

- Pathogenesis: **autoimmune** etiology
- Note: distinction from giant cell aortitis is made on the patient's **age**:
- >50 years → giant cell aortitis
- **<50 years** → Takayasu aortitis.

- Treatment: immunosuppressives

Takayasu arteritis -MORPHOLOGY



Kumar et al: Robbins Basic Pathology, 9e.

3- Kawasaki disease

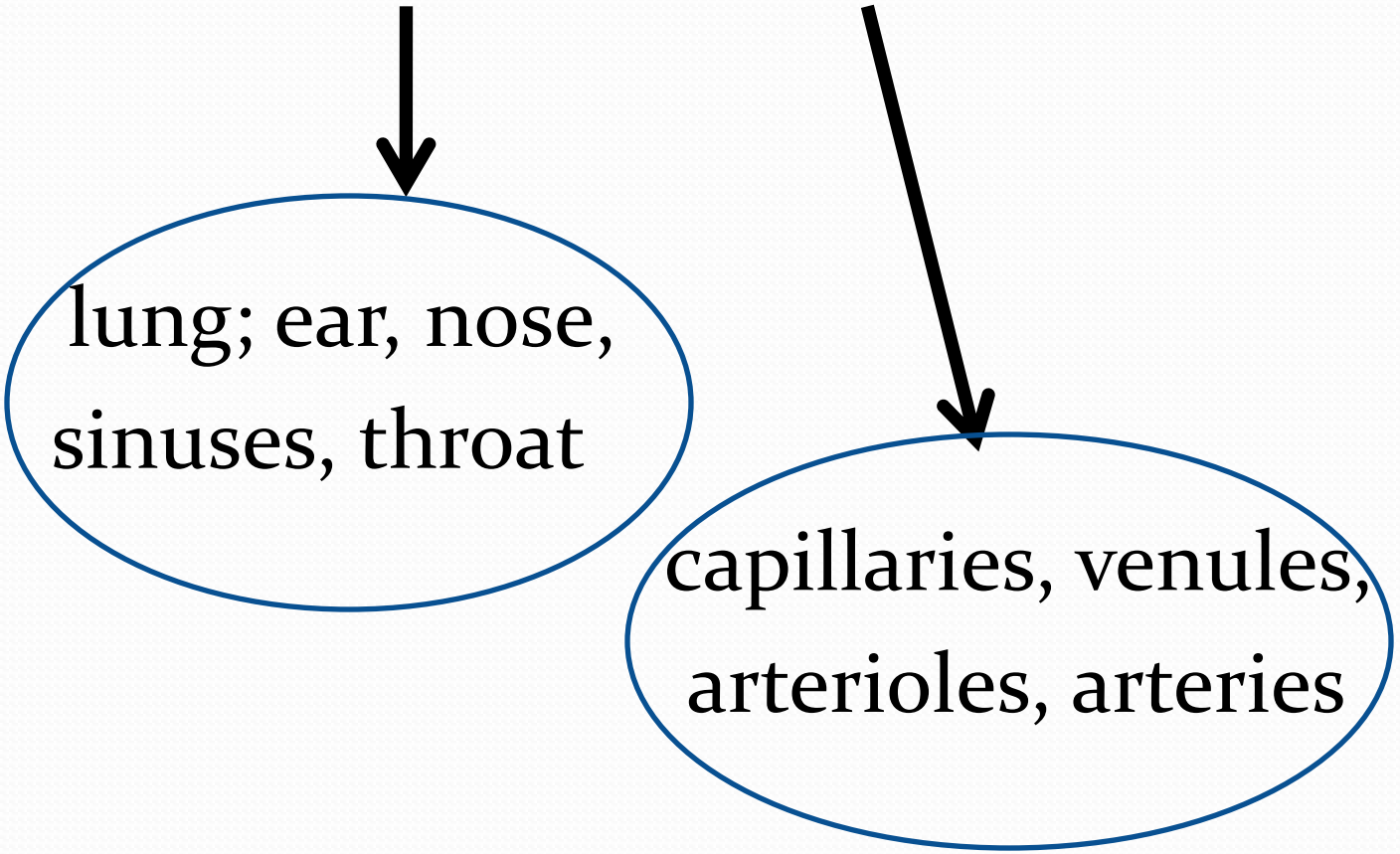
- Acute febrile illness of **childhood** (80% < 4 yr)
- **large to medium-sized** arteries.
- Also called ***mucocutaneous lymph node syndrome***
- ***coronary arteries*** → aneurysms → rupture or thrombosis→ **myocardial infarction in a child**.
- Originally in Japan, but now recognized worldwide

- Other symptoms:
- conjunctival & oral erythema and blistering
- erythema of palms and soles
- desquamative rash
- cervical lymph node enlargement

- Pathogenesis: **anti-endothelial cell antibodies**
- *Treatment*: intravenous immunoglobulin therapy and aspirin

4- Wegener granulomatosis

- triad: **granuloma+ vasculitis + glomerulonephritis:**



Wegener granulomatosis-

- **pathogenesis : c-ANCA** 95%
- **Treatment**: steroids, cyclophosphamide, TNF inhibitors…
- high risk for relapses
- **If untreated, mortality rate at 1 year 80%.**

5- Churg-Strauss syndrome

- a small vessel vasculitis
- asthma, allergic rhinitis, lung infiltrates, peripheral eosinophilia, necrotizing granulomas, eosinophils.
- extremely rare disorder.
- Pathogenesis: p-ANCA associated

6- Thromboangiitis obliterans (Buerger disease)

- vascular insufficiency & **gangrene** of **fingers and toes**.
- medium-sized & small arteries (**tibial and radial**)
- **secondary extension into adjacent veins and nerves may be seen.**
- ***Pathogenesis***: **heavy tobacco smokers** and usually **< age 35** {components of tobacco- ? Direct endothelial cell toxicity ? -an immune response -? A genetic predilection}
- ***Treatment*: Smoking abstinence in early stages**

Vasculitis	Pathogenesis	Major vessels affected	Clues
Giant cell arteritis	T cell-mediated	temporal arteries; vertebral; ophthalmic ; aorta	Granulomas; blindness
Takayasu Arteritis	؟Autoimmune	aortic arch	"pulseless disease"
Kawasaki disease (mucocutaneous lymph node syndrome)	anti-endothelial cell Ab	coronary arteries	Myocardial infarction in a child
Wegener granulomatosis	c-ANCA	medium-sized vessels	granuloma+vasculitis + glomerulonephritis
Churg-Strauss syndrome	p-ANCA	small vessel	asthma, allergic rhinitis, peripheral eosinophilia
Thromboangiitis obliterans (Buerger disease)	tobacco smoking	tibial and radial arteries; adjacent veins and nerves	Gangrene of fingers and toes