The Cardio-VASCULAR System

- ○ Anatomy
- ○ Histology
- ● Pathology
- ○ Pharmacology
- ○ Physiology
- ○ Microbiology

Lec #: 7

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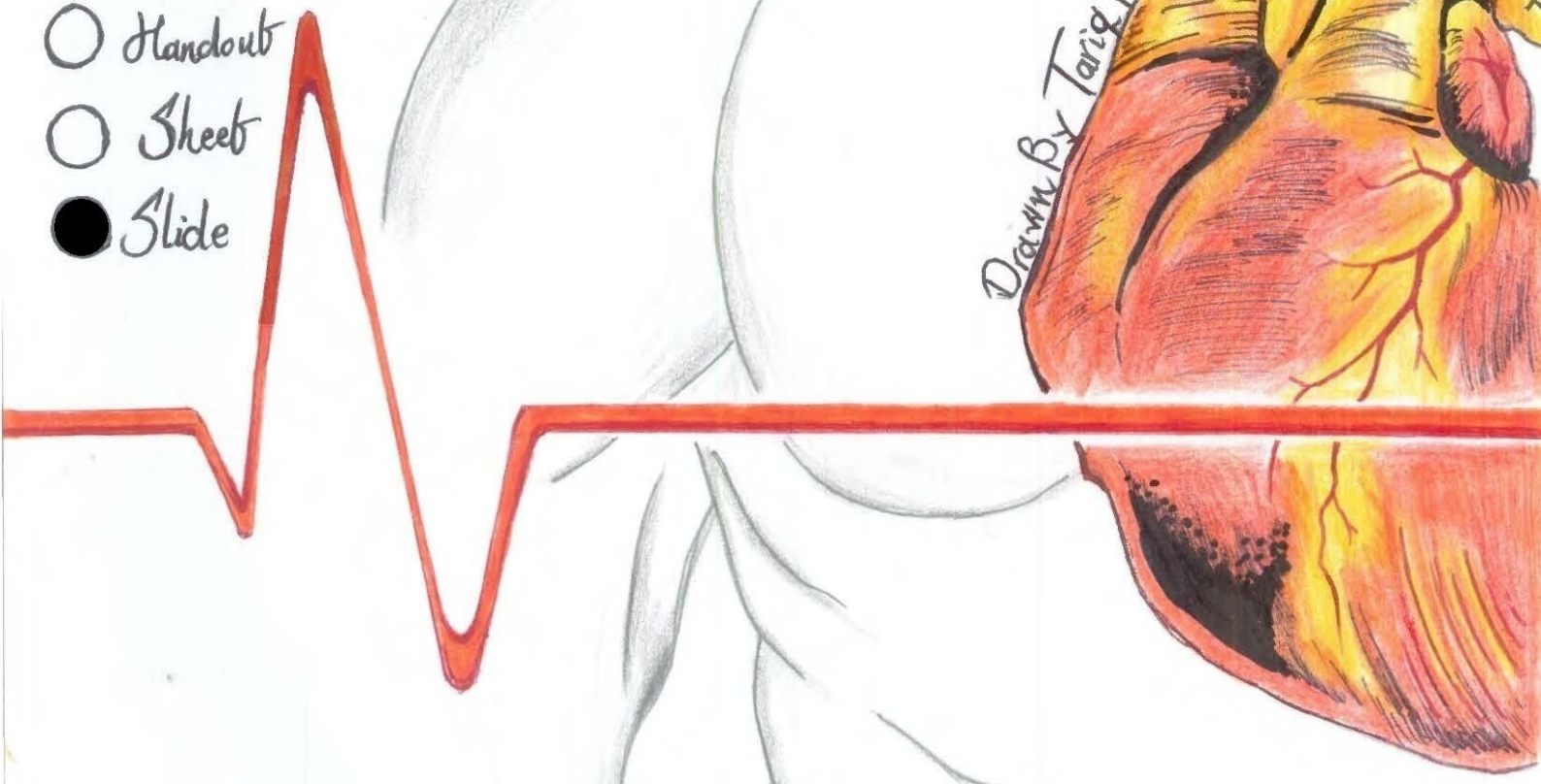
Done By:

- ○ Handout
- ○ Sheet
- ● Slide



Vasculitis

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

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

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

Pathogenesis

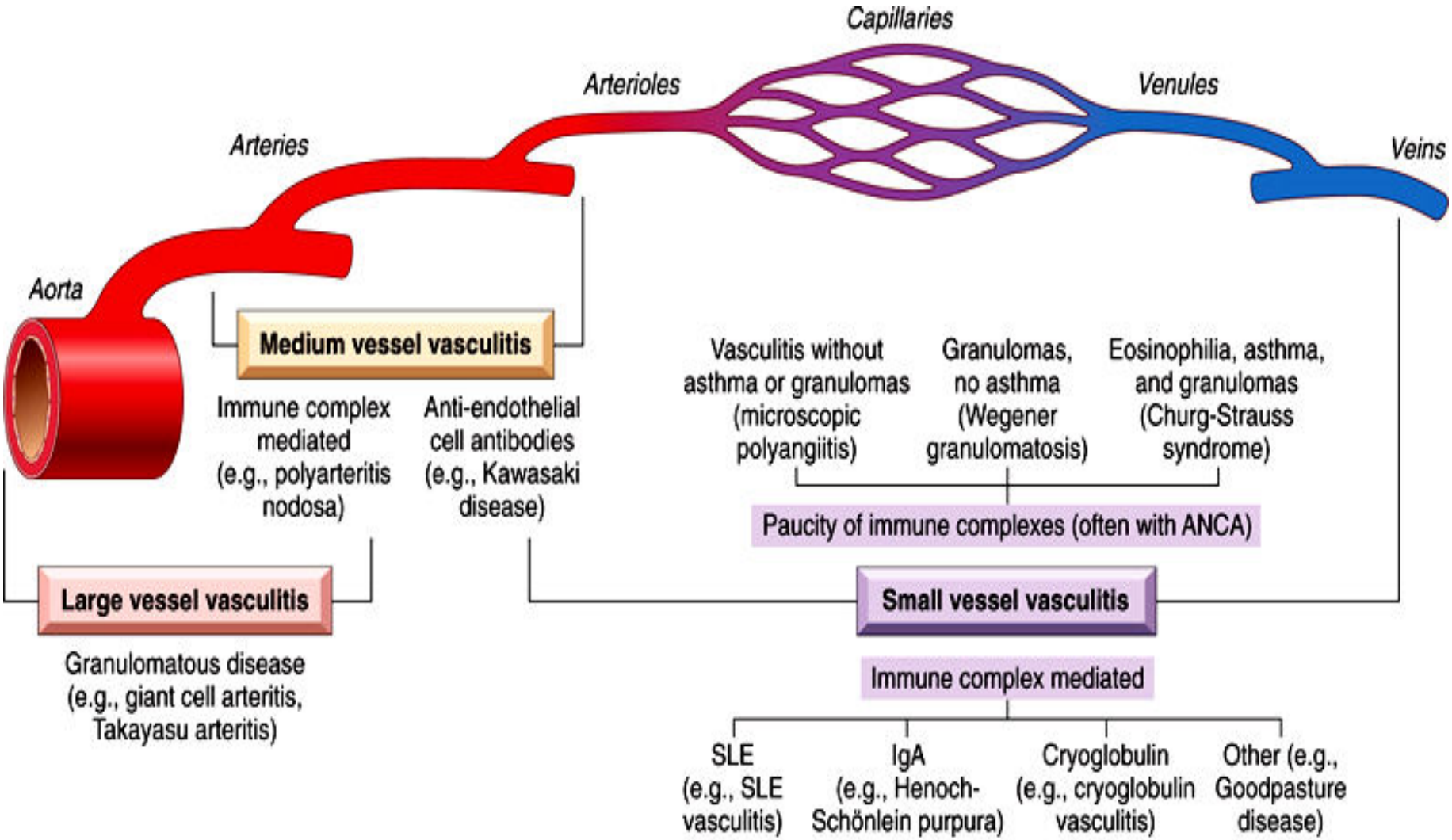
1- immune-mediated inflammation

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.

- **The main *immunologic mechanisms* underlying vasculitis are:**

1- **Immune complex** deposition

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

3-**Anti-endothelial cell antibodies**

4-**Auto-reactive T cells**

Immune complex deposition

- Example:

Drug 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.

Anti-Neutrophil Cytoplasmic Antibodies

- **ANCAs** = circulating antibodies that react with neutrophil cytoplasmic antigens (mainly enzymes)
- ANCAs blood levels are very useful markers for diagnosis, clinical severity, and as predictive of disease recurrence.

- two types are most important:

1- Antiproteinase-3 (PR3-ANCA)= **c-ANCA**.

- ***proteinase-3*** is a neutrophil azurophilic granule constituent;
- e.g. Wegener granulomatosis.

2-Anti-myeloperoxidase (MPO-ANCA)= **p-ANCA**.

- MPO is a lysosomal granule constituent;
- e.g. Churg-Strauss syndrome

Anti-Endothelial Cell Antibodies

- Antibodies against endothelial cells
- Associated with certain vasculitides, such as Kawasaki disease (discussed later).

Giant Cell (Temporal) Arteritis

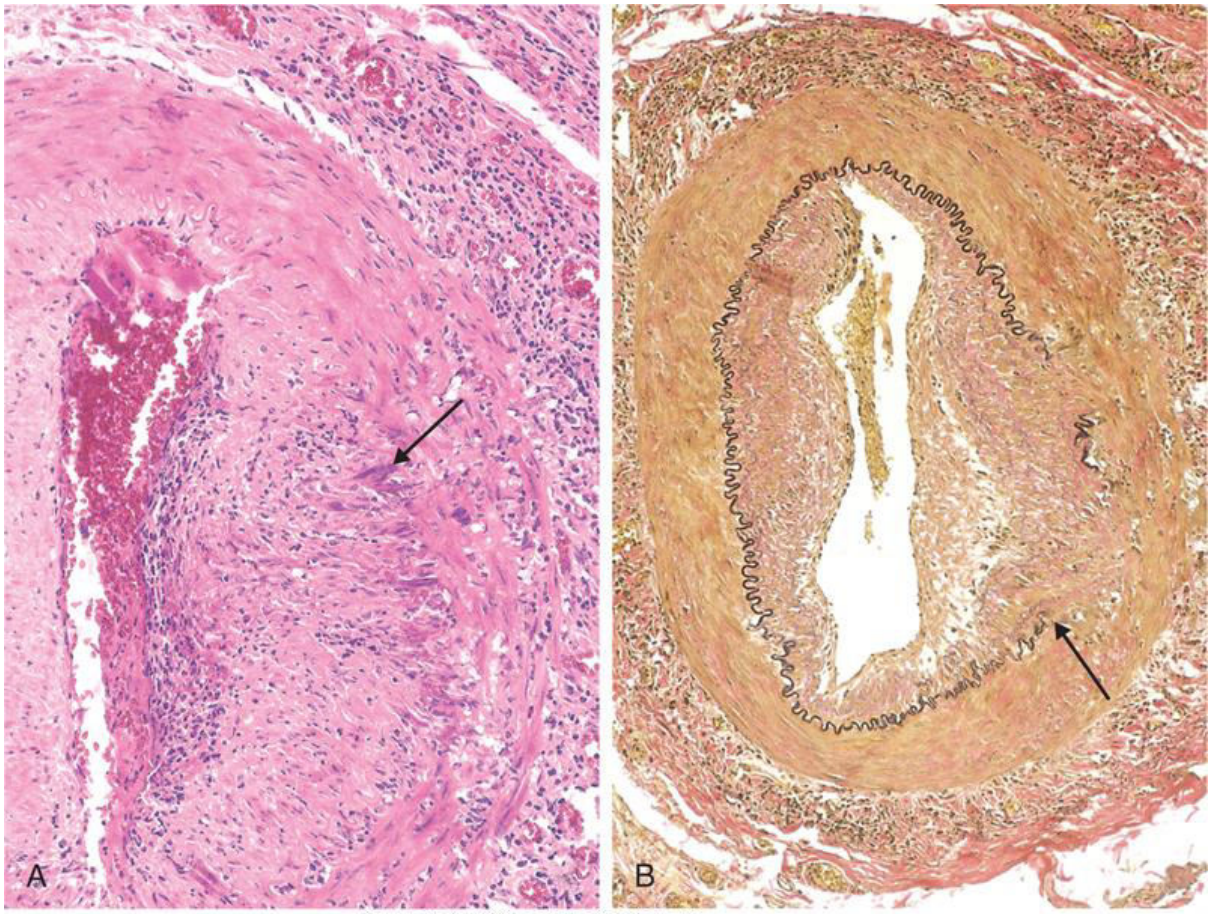
- ***is the most common form of vasculitis among the elderly in developed countries.***
- *chronic,* ***granulomatous****, inflammation of large arteries*
- *mainly the* ***temporal arteries****, ve*rtebral and ophthalmic arteries, as well as the aorta also can be involved.
- ophthalmic artery involvement→ sudden and permanent **blindness** (rapid diagnosis and treatment are mandatory)

Giant Cell (Temporal) Arteritis

- ***Pathogenesis*: T cell-mediated immune response to unknown vessel wall antigen.**
- ***Morphology*:**
- **granulomatous inflammation (75%) within the inner media centered on the internal elastic membrane ((lymphocytes and macrophages, with multinucleate giant cells))**
- **fragmentation of the internal elastic lamina.**
- **lesions at different stages of development are seen within the same artery**

Giant Cell (Temporal) Arteritis:

A> granuloma; B> fragmented internal elastic lamina



Giant Cell Arteritis- clinical picture

- rare before the age of 50.
- ***Signs and symptoms:***
- fever, fatigue, weight loss
- facial pain or headache (superficial temporal artery).
- Ocular symptoms (ophthalmic artery) in 50% of patients; range from diplopia → → complete vision loss.
- ***Diagnosis***:

- Vessel biopsy and histology

- ***Treatment***:

- Corticosteroid or anti-TNF therapies

Takayasu Arteritis

- vasculitis of medium-sized and large arteries

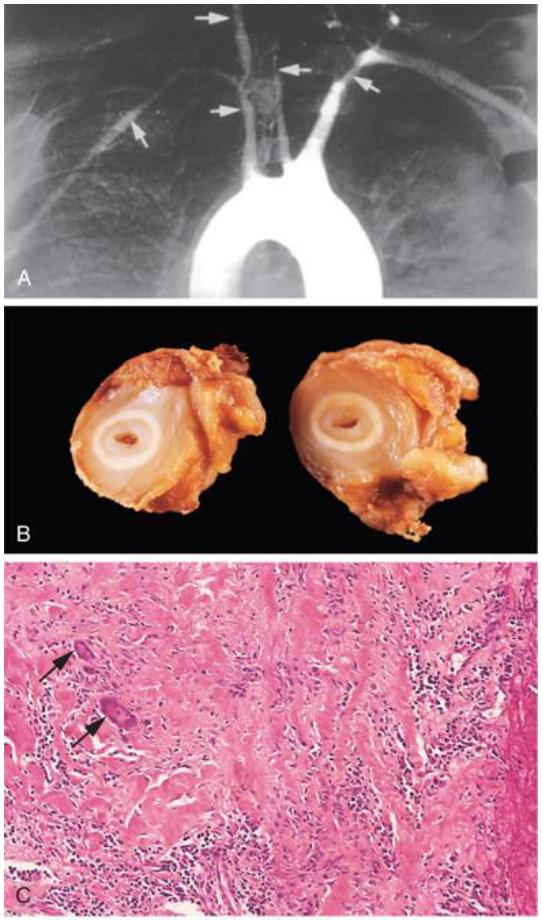
- **scarring** and thickening of the **aorta-** especially the **aortic arch** with severe luminal narrowing of the major branch vessels.

- marked weakening of the pulses in the upper extremities **(= the pulseless disease).**

Takayasu arteritis

- Pathogenesis: An **autoimmune** etiology is likely
- **affects the aortic arch and arch vessels (2/3)**
- the distinction from giant cell aortitis is made largely on the basis of a patient's age: >50 years →giant cell aortitis **<50 years**→Takayasu aortitis.
- Treatment: immunosuppressives

Takayasu arteritis -MORPHOLOGY



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Polyarteritis nodosa (PAN)

- a systemic vasculitis of *small or medium-sized muscular arteries*
- typically involves the **renal** and **visceral** vessels and ***spares*** the pulmonary circulation.
- There is **no** association with ANCAs

- **(1/3) chronic hepatitis B infection→ immune complexes containing hepatitis B antigens deposit in affected vessels**.
- (2/3) →The cause is unknown

PAN- The clinical course

- **episodic, with long symptom-free intervals.**
- **malaise, fever, and weight loss**
- **the vascular involvement is widely scattered.**
- **Usually present as a combination of:**

- **malignant hypertension → a major cause of death**
- **abdominal pain and bloody stools (GIT lesions)**
- **muscular aches and pains**
- **peripheral neuritis.**

- **Treatment: if untreated → fatal**

  - immunosuppression →remission or cure in 90% of the cases

Kawasaki disease

- acute, febrile illness of infancy and **childhood** (80% of cases < 4 years)
- arteritis of mainly **large to medium-sized** vessels.
- *Its clinical significance: involvement of* ***coronary arteries*** ➔ aneurysms → rupture or thrombosis→ **myocardial infarction**.
- Originally in Japan, the disease is now recognized worldwide

- Also called ***mucocutaneous lymph node syndrome:***

- conjunctival and oral erythema and blistering
- erythema of the palms and soles
- a desquamative rash
- cervical lymph node enlargement

- Pathogenesis: **anti-endothelial cell antibodies**
- *Treatment*:

- intravenous immunoglobulin therapy and aspirin

Wegener granulomatosis

- a necrotizing vasculitis with a specific triad of:

1- ***Granulomas*** of the lung and/or the upper respiratory tract (ear, nose, sinuses, throat)

2- ***Vasculitis*** of small to medium-sized vessels (capillaries, venules, arterioles, and arteries) mostly in **lungs** and **upper respiratory tract**

3- **renal** *vasculitis (**Glomerulonephritis):***

Wegener granulomatosis-pathogenesis

- PR3-ANCAs (**c-ANCA**) is detected > 95% of cases

  - useful markers of disease activity (After immunosuppressive therapy, ANCA levels fall dramatically, while rising titers are predictive of relapse)

- **The typical patient is >40 year old and male, although women and all ages can be affected.**
- **If untreated, the mortality rate at 1 year is 80%.**

Wegener granulomatosis- clinical picture

- Rash, myalgias, articular involvement, neuritis, and fever
- bilateral pneumonitis, nodules and cavitary lesions (95%)
- chronic sinusitis (90%)
- mucosal ulcerations of nasopharynx (75%)
- renal disease (80%)➔→→ rapidly progressive renal failure.
- *Treatment*: steroids, cyclophosphamide, TNF inhibitors...
- Most patients with Wegener granulomatosis now survive, but remain at high risk for relapses that can ultimately lead to renal failure.

Churg-Strauss syndrome

- **is a *small vessel necrotizing vasculitis***
- *classically associated with* **asthma, allergic rhinitis, lung infiltrates, *peripheral eosinophilia, necrotizing granulomas, infiltration by eosinophils***.
- extremely rare disorder.
- purpura, GIT bleeding, and renal disease are the major associations.
- Cardiomyopathy (60% of patients)→ a major cause of morbidity and death.
- Pathogenesis: **p-ANCA** associated

Thromboangiitis obliterans (Buerger disease)

- a disorder of severe vascular insufficiency and **gangrene** of the extremities.
- focal acute and chronic inflammation of medium-sized and small arteries, especially the **tibial and radial arteries**, associated with thrombosis
- **secondary extension into adjacent veins and nerves may be seen.**
- *Pathogenesis*: almost exclusively in **heavy tobacco smokers** and usually **< age 35**.
- The etiology is unknown:- components of tobacco- ? Direct endothelial cell toxicity ? -an immune response.

  -? A genetic predilection

Thromboangiitis obliterans/clinical manifestations

- Early : Raynaud phenomenon, foot pain induced by exercise, superficial nodular phlebitis (venous inflammation).
- severe pain-even at rest→ neural involvement.
- Chronic ulcerations
- Gangrene of fingers and toes
- ***Treatment***: Smoking abstinence in the early stages of the disease