Pathology team 441

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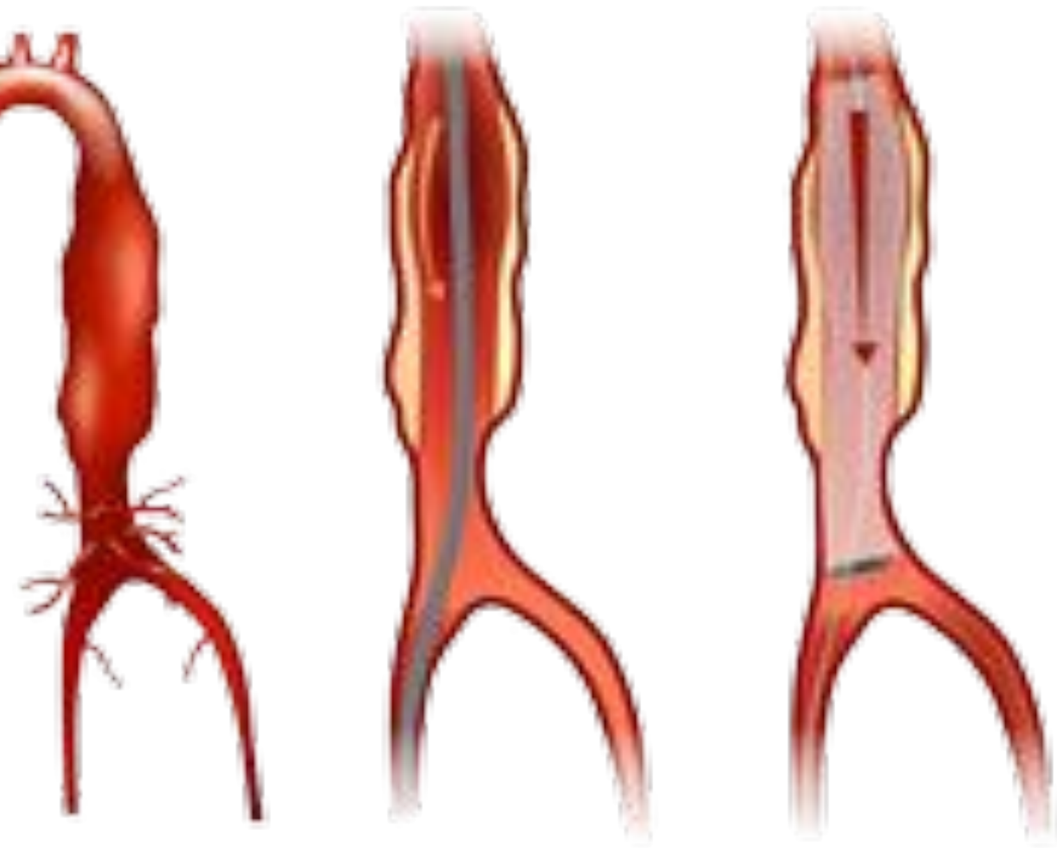
MED441
KING SAUD UNIVERSITY

Vasculitis



Editing File

Color Index:

- Main text
- **Important**
- Boys slides
- Girls slides
- Dr's notes
- Extra

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:

1. Giant cell arteritis.
2. Polyarteritis nodosa.
3. Wegener's granulomatosis.
4. Cutaneous hypersensitivity vasculitis.
5. Thromboangiitis obliterans (Burger’s disease)

Introduction: Vasculitis

Vasculitis

It is a general term for inflammation of vessel walls of arteries (more common) and veins, has **many** possible symptoms (depending on the vessel it's affecting) and often with necrosis

Causes of Vasculitis

Immune-mediated (Most common)

Main immunological mechanisms:

- Immune complex deposition
- Antineutrophil cytoplasmic antibodies (ANCAs) (antibodies against cytoplasmic neutrophils)
- Anti-endothelial cell antibodies
- Autoreactive T cells

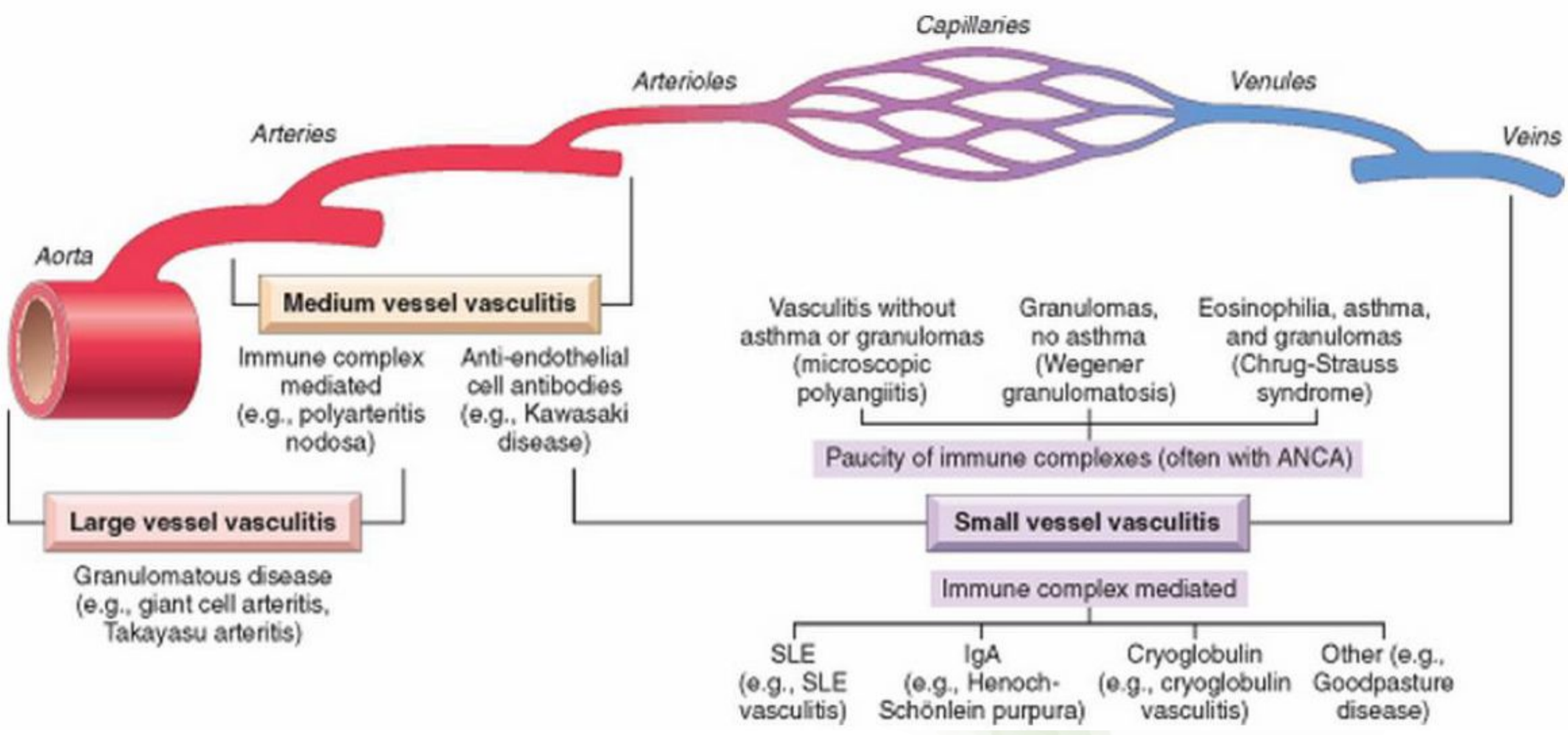
Invasion of vascular walls by

- Infectious pathogens
- Physical or chemical injury

Overview: Types of Vasculitis

They are grouped according to the size of blood vessels affected.

Vessel	Disease	Notes
Large	**Giant-cell arteritis**	>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.
	Cutaneous leukocytoclastic vasculitis	Idiopathic, infectious, drugs, chemicals, cancer and systemic disease like HNP



Antineutrophil Cytoplasmic Antibodies (p-ANCA) Male slides

Cytoplasmic localization (c-ANCA)

The most common target antigen is proteinase-3 (PR3)

Typical of Wegener granulomatosis

Perinuclear localization (p-ANCA)

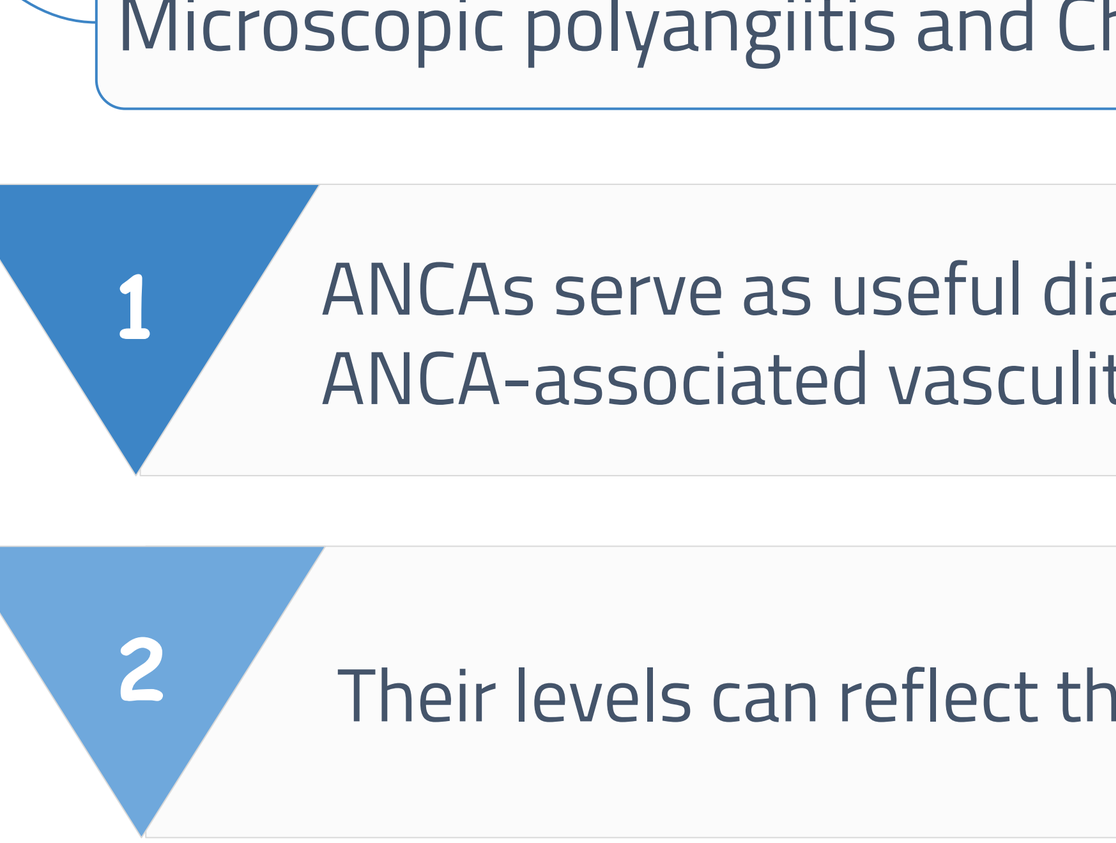
Most of the autoantibodies are specific for myeloperoxidase (MPO)

Microscopic polyangiitis and Churg-Strauss syndrome

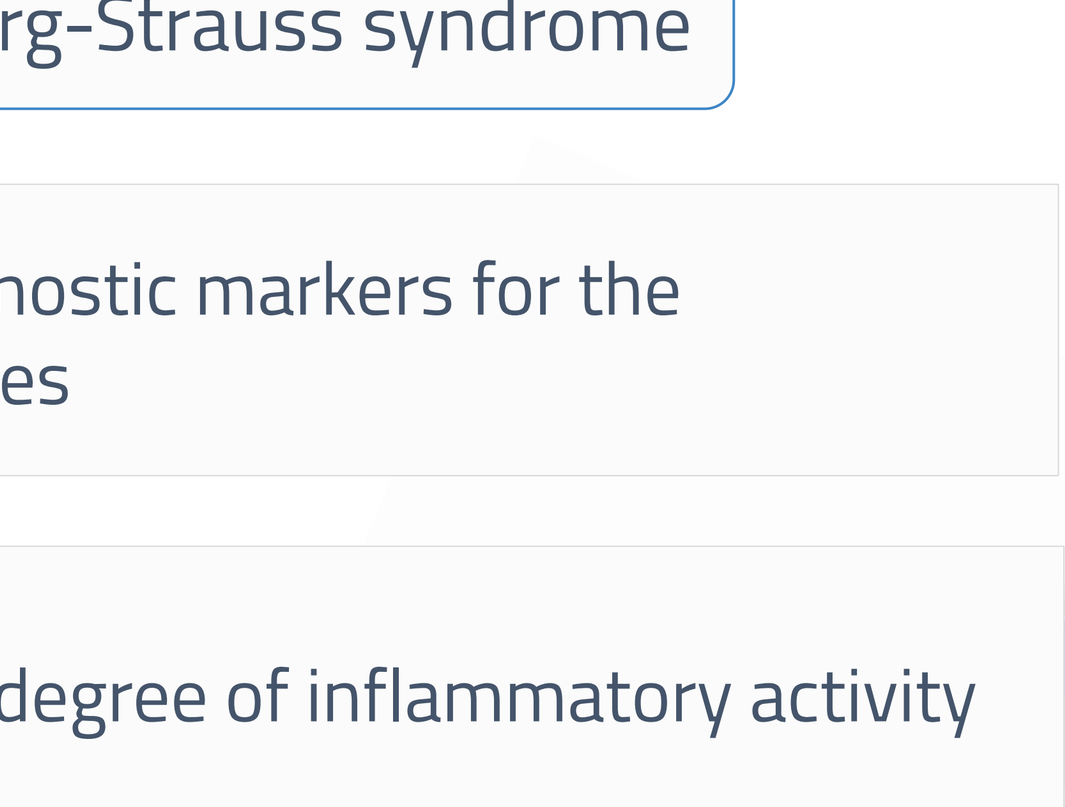
1. ANCAs serve as useful diagnostic markers for the ANCA-associated vasculitides

2. Their levels can reflect the degree of inflammatory activity

c-ANCA



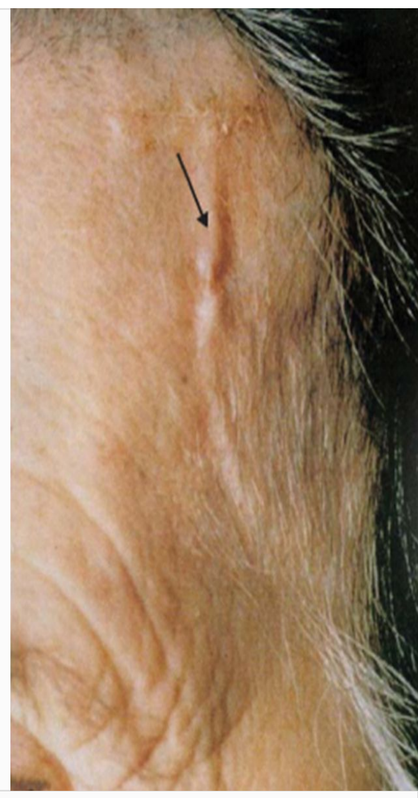
p-ANCA



Giant-Cell (Temporal) Arteritis

Definition

Chronic, granulomatous inflammation of large to medium sized arteries (large to small-sized arteries), especially the **branches of the carotid artery** in the head (**temporal artery** and branches of the ophthalmic artery), rarely the aorta (giant-cell aortitis). The involvement is segmental,not the whole artery is affected. The inflammation could be acute and chronic.

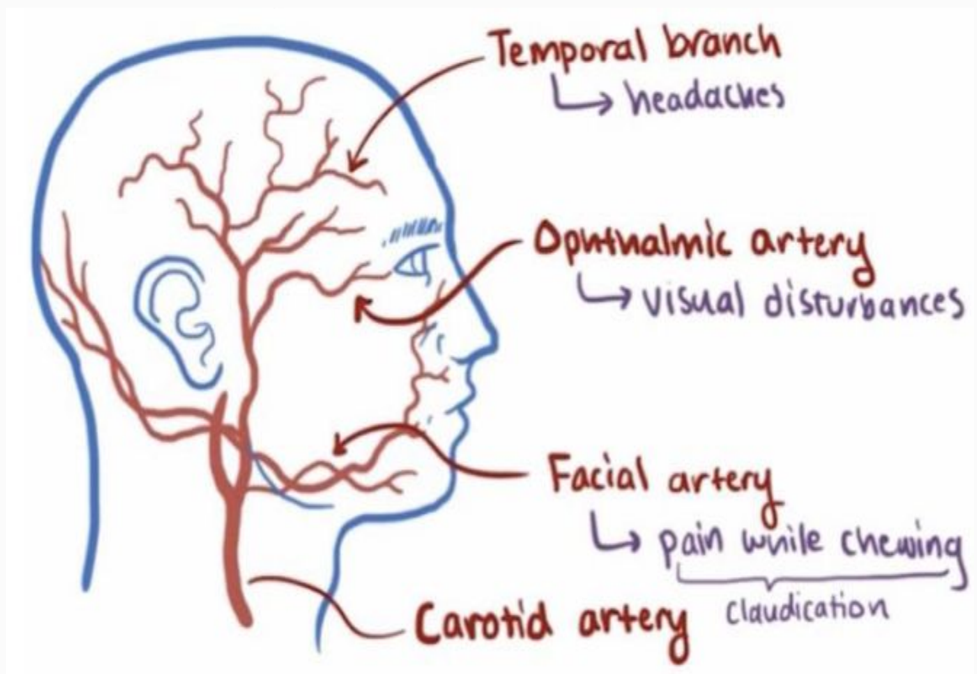


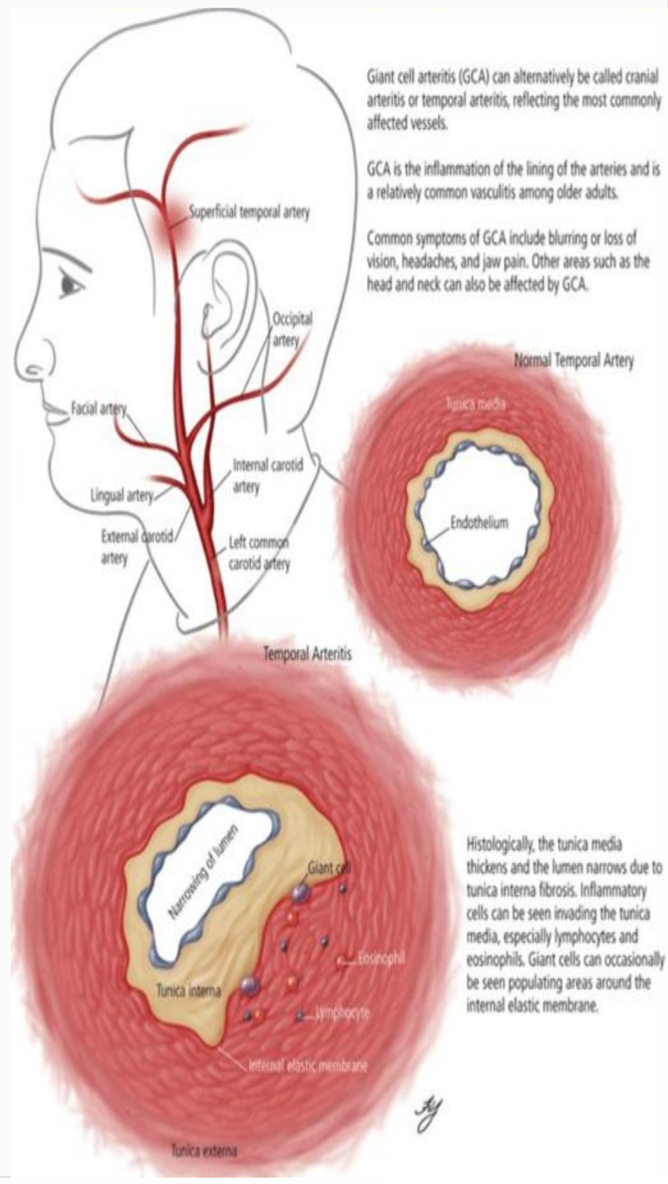
Epidemiology

- Most common type of vasculitis
- Unknown cause, But it is probably an autoimmune condition. T cell-mediated
- **Above 50 years old**
- **More common in females** (F:M, 2:1)

Symptoms
Clinical features

- **Fever.**
- **Facial pain or headache,** often most intense along the course of the superficial **temporal artery.** which is painful to palpation
- Visual problems and acute vision loss (due to ophthalmic artery involving)
- Thickened and painful temporal artery.
- Jaw pain.
- Vague symptoms:
  – Fever, fatigue and weight loss





Giant-Cell (Temporal) Arteritis

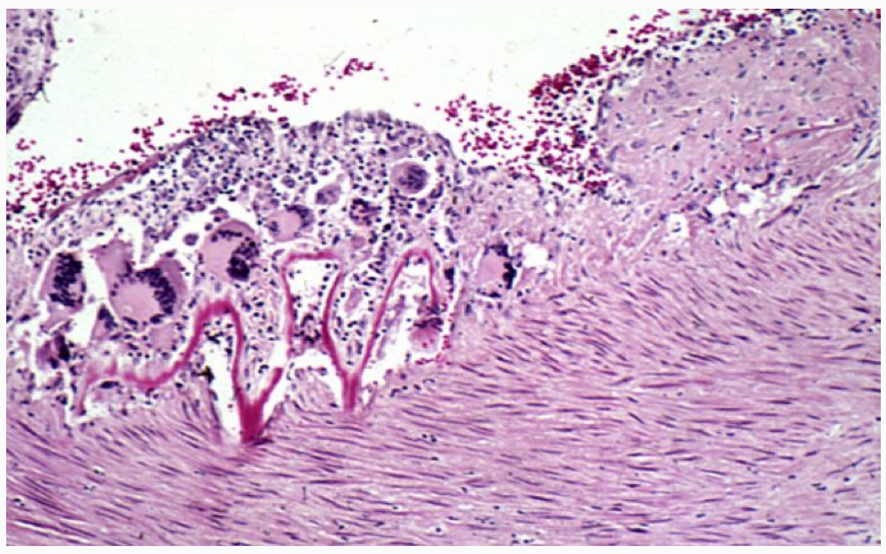
Diagnosis & Treatment

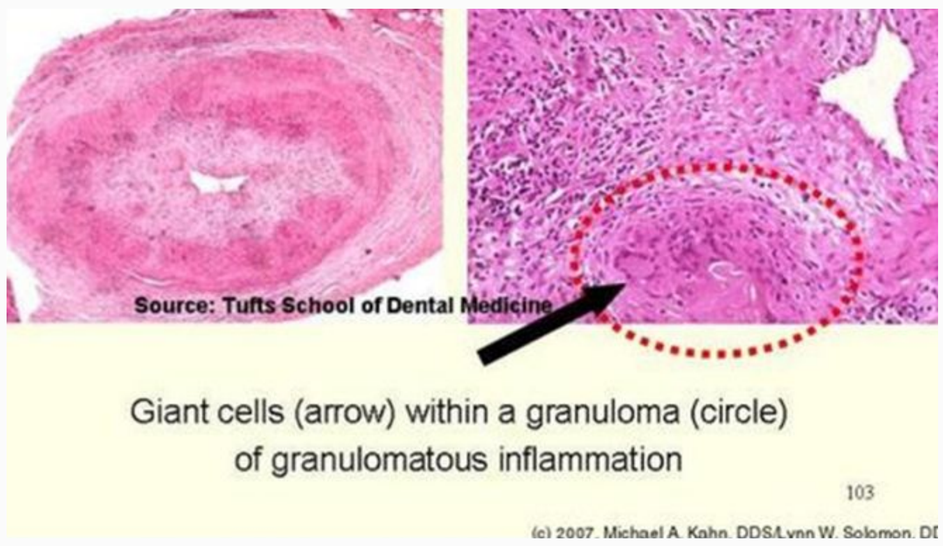
439 note: Clinical index of suspicion that leads to obtaining a biopsy from affected area. As its segmental sometimes biopsies are negative since not the whole vessel is diseased.

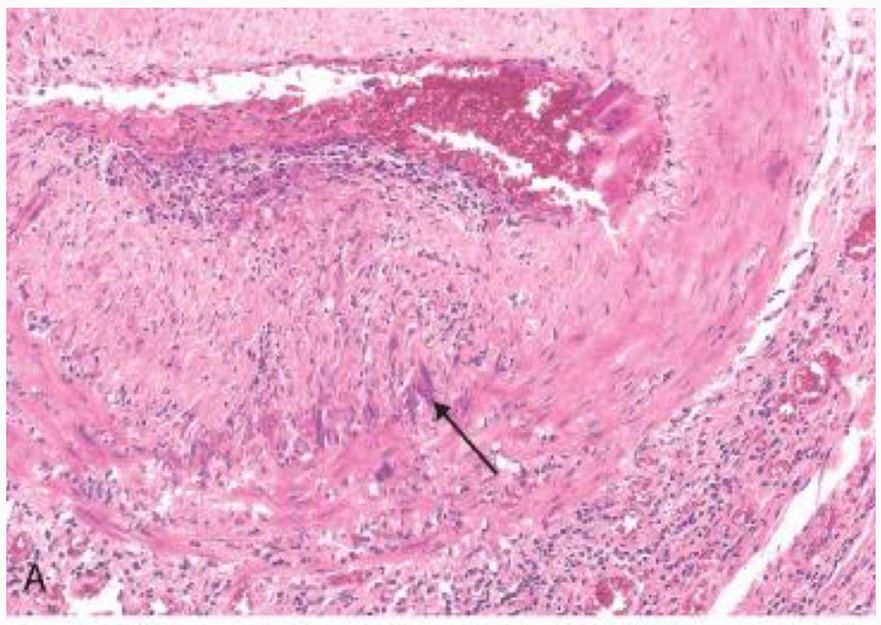
- The diagnosis depends on biopsy (from the temporal artery) and histologic confirmation.
- Treatment - corticosteroids (weakens immune response)

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.







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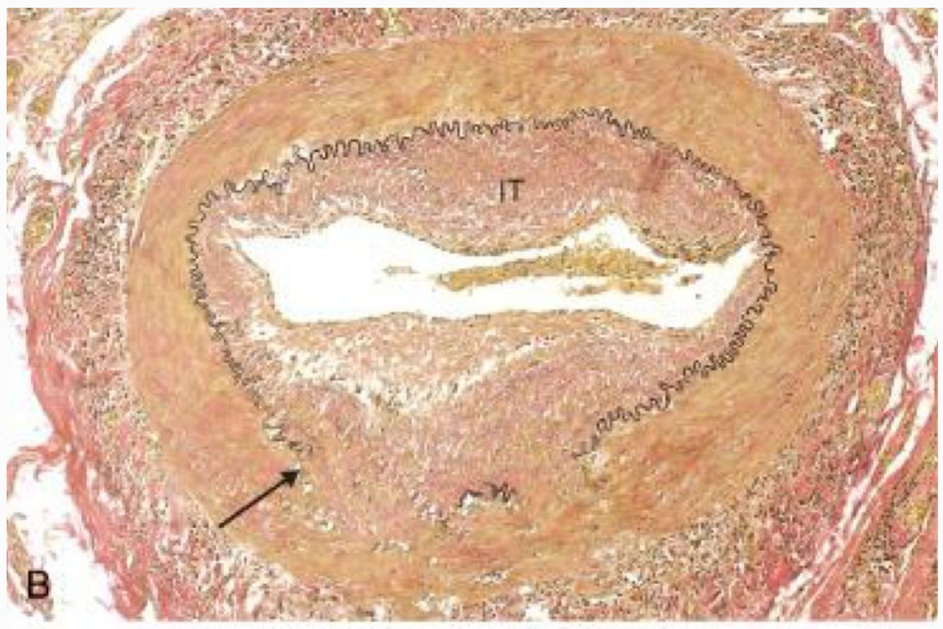

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Polyarteritis Nodosa (PAN)

Definition

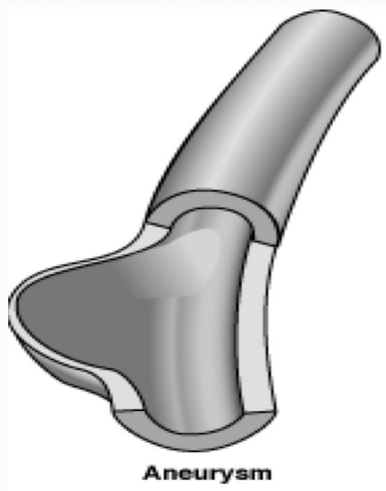
Segmental (nodosa= nodes) necrotizing inflammation of arteries of **medium to small size,** but **not** arterioles, capillaries, or venules could involve any organ (renal and visceral vessels) except the lungs (pulmonary circulation).

Epidemiology

It’s a disease of young adults.

Characteristics

- Most frequently **kidneys** (most common, so renal manifestations are seen), heart, liver, and gastrointestinal tract.
- Renal arterial involvement is often prominent and is a **major cause of death.**
- PAN been associated with **hepatitis B** or **hepatitis C virus** infection. The immune cells attack the endothelium rather than hepatitis B and causing transmural inflammation (all 3 layers of vessel are affected). 439 note
- **Weakening of the arterial wall** due to the inflammatory process may cause **aneurysmal** dilation or localized rupture.



- 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.
- **No** association with ANCA (antineutrophil cytoplasmic antibodies)
- Typically episodic, with long symptom-free intervals
- Because the vascular involvement is widely scattered, the clinical findings may be varied and puzzling

Polyarteritis Nodosa (PAN)

Diagnose & Treatment

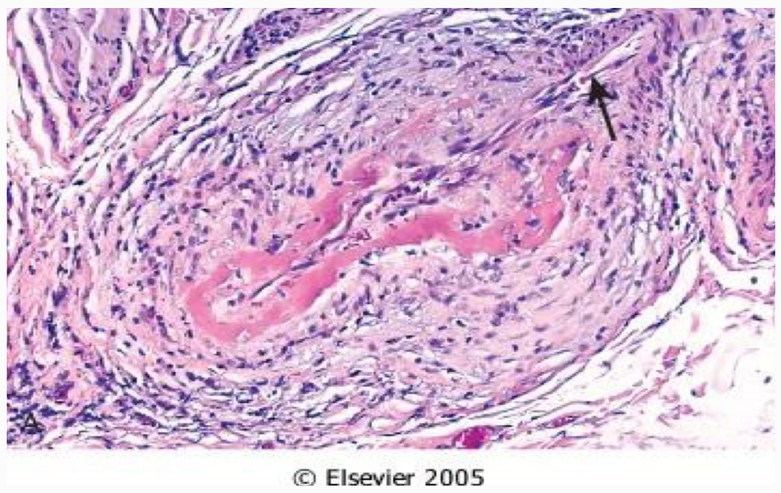
- Biopsy is often necessary to confirm the diagnosis
- Fatal if untreated, but steroids, cyclophosphamide and other immunosuppressive therapy results in remissions or cures in 90%

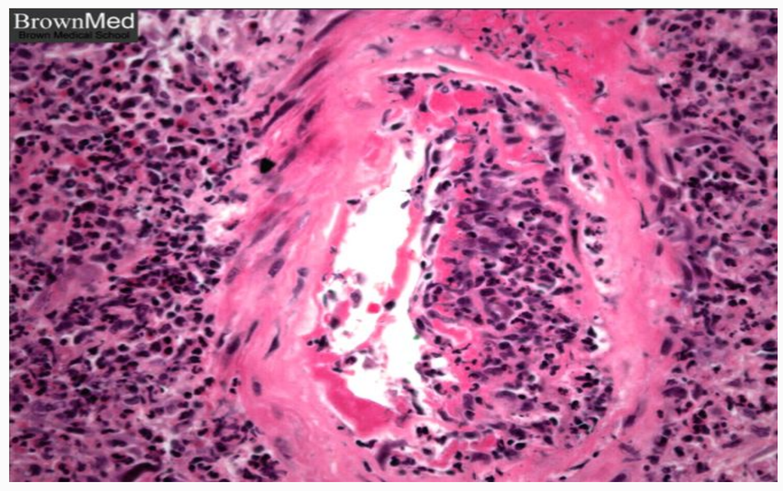
Complications

- Vessel rupture
- Impaired perfusion:
- Ulcerations
- Infarcts
- Ischemic atrophy (not infarction)
- Haemorrhages in the distribution of affected vessels may be the first sign of disease

Morphology

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.

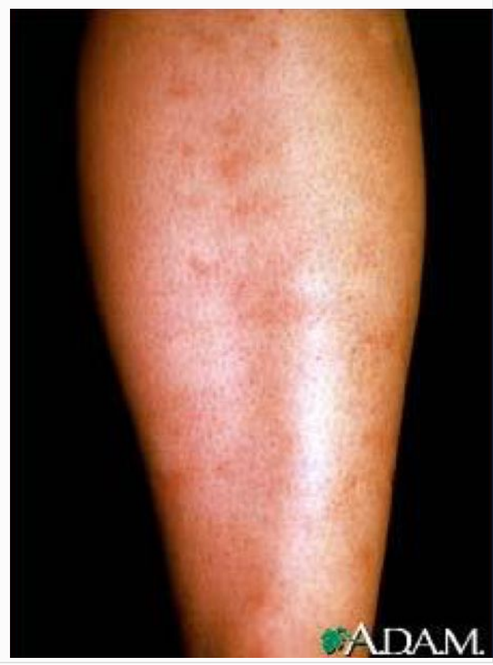




Symptoms (Clinical features)

Manifestations are due to **ischemia and infarction** of the affected tissue/organ:

- Fever
- Weight loss
- Abdominal pain
- Melena (bloody stool)
- Muscular pain
- Peripheral neuritis
- Hypertension, usually developing rapidly



Granulomatosis with Polyangiitis (Previously: Wegener granulomatosis)

Definition	A type of necrotizing vasculitis affecting small-medium sized vessels characterized by wegener's triad. The name highlights the two central pathologic features of the disease, granuloma formation and inflammation of blood vessels. (Uncommon disease)
Epidemiology	Males are affected more often than females, at an average age of about 40 years.
Diagnosis	Wegener's triad is a pathomorphological diagnostic criteria that states the involvement of: 1. Necrotizing granulomas of the upper (nose,pharynx, etc) and lower respiratory tract (lung) 2. Renal disease (kidney involvement) in the form of necrotizing, crescentic, glomerulonephritis 3. Necrotizing or granulomatous vasculitis of small to medium sized vessels.

Granulomatosis with Polyangiitis (Previously: Wegener granulomatosis)

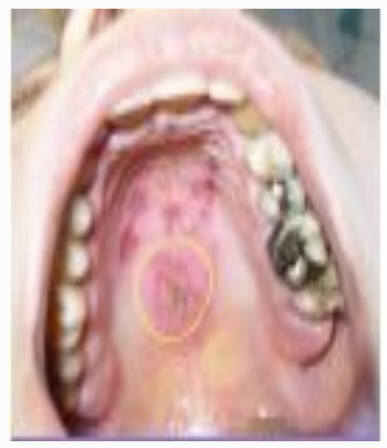
Prognosis

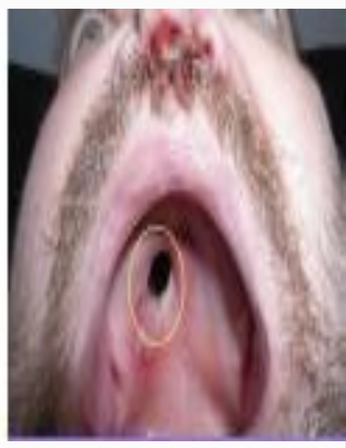
Untreated = fetal
May lead to death within 2 years if not treated.

Symptoms
Clinical features

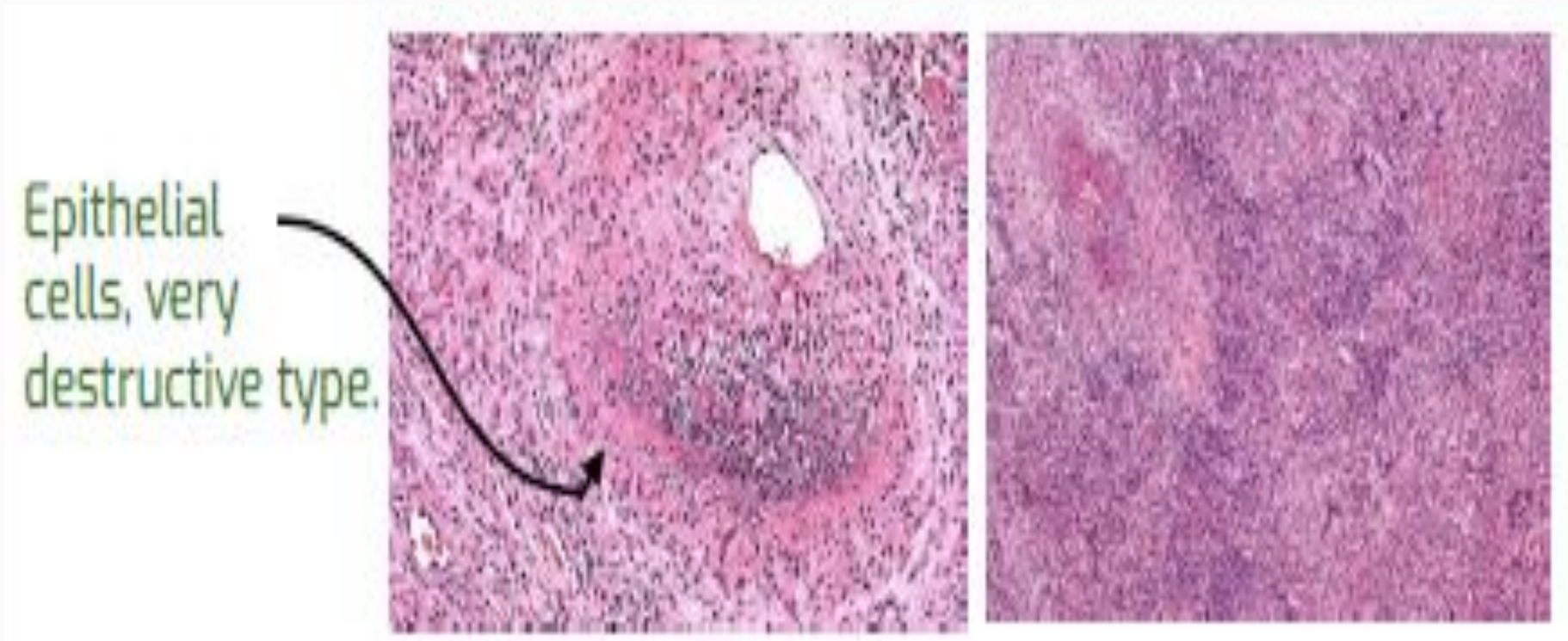
Remember that manifestations depend on the organs affected by this type of vasculitis.

- Chronic sinusitis (URT)
- Mucosal ulcerations of the nasopharynx (URT)
- Persistent pneumonitis (LRT)
- Evidence of renal disease
- C-ANCAs (antineutrophilic cytoplasmic antibodies) is positive in serum of more than 95% of patients.





Morphology



Microscopic polyangiitis / polyarteritis

Definition

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

Clinical features

- **P-ANCA** is characteristically present
- In the past it has been confused with leukocytoclastic vasculitis

Churg-Strauss syndrome (additional reading)

Definition

Eosinophil-rich and granulomatous inflammation involving the respiratory tract and necrotizing vasculitis affecting small vessels.

Clinical features

- Associated with **P-ANCAs**
- Associated with asthma and blood eosinophilia

Cutaneous leukocytoclastic (hypersensitivity vasculitis/ angiitis)

Definition

- **Necrotizing vasculitis** of arterioles, capillaries, venules .
- Inflammation of small blood vessels.
- Leukocytoclasis refers to the nuclear debris of infiltrating neutrophils in and around the vessels.

Characteristics

- It is the most common vasculitis seen in clinical practice.
- It affects many organs e.g. skin (most common), mucous membranes, lungs , brain, heart, GI , kidneys and muscle.
- commonly seen in the dermis of skin characterized by **palpable purpura**.
- All lesions tend to be of the same age.

Etiology

- 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**

Henoch-Schonlein purpura (HSP)

Definition

is an **IgA**-mediated, autoimmune systemic disease in which the small vessels show leukocytoclastic vasculitis.

- Unknown cause

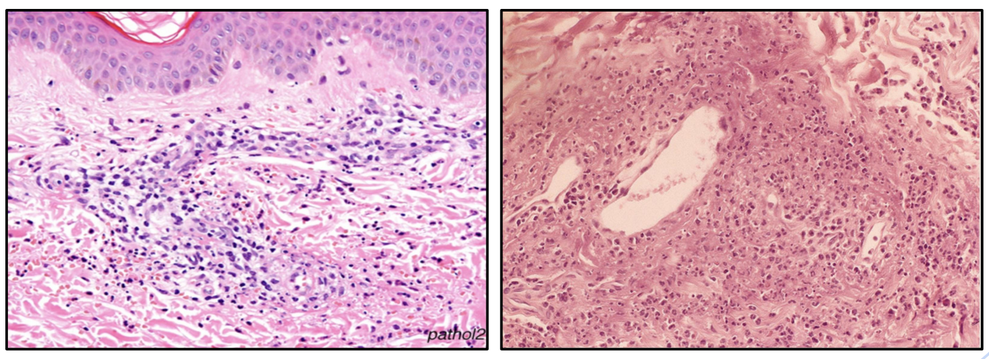
Characteristics

- 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.

Investigation
(Skin biopsy is often diagnostic)

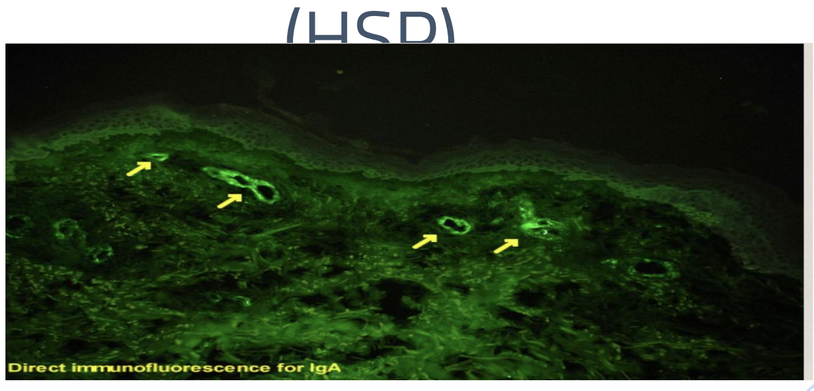
Microscopically

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



direct immunofluorescence

will show **deposits of IGA** immunoglobulin in the wall the capillaries in Henoch-Schonlein purpura (HSP)



Thromboangiitis obliterans (Buerger disease)

Characteristics

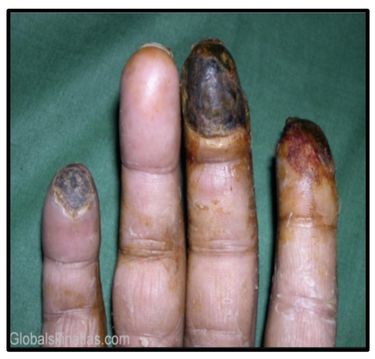
Segmental, thrombosing, acute and chronic inflammation of **medium-sized and small arteries**, principally of the leg and hands (tibial and radial arteries) with secondary extension into adjacent veins and nerves.

Risk factors

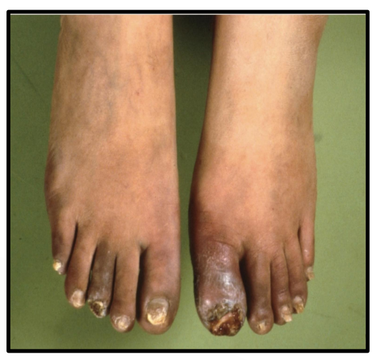
- Buerger disease is a condition that occurs almost exclusively in **heavy smokers** of cigarettes
- Patients are usually **under 35** years of age.
- Tobacco either leads to **direct toxicity** to endothelium, or induces an immune response

Clinical features

- pain in the affected hand or foot **induced by exercise** (called **instep claudication**).even at rest, due to the neural involvement.

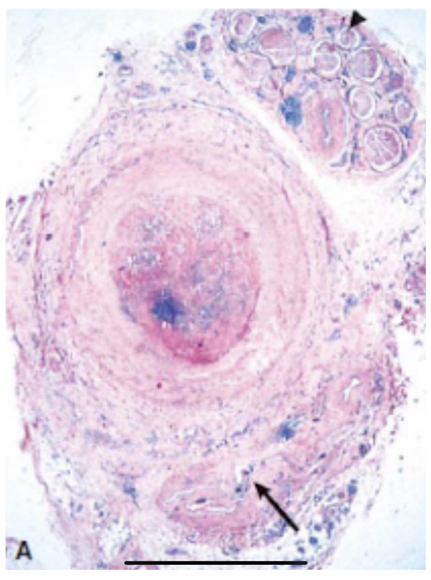


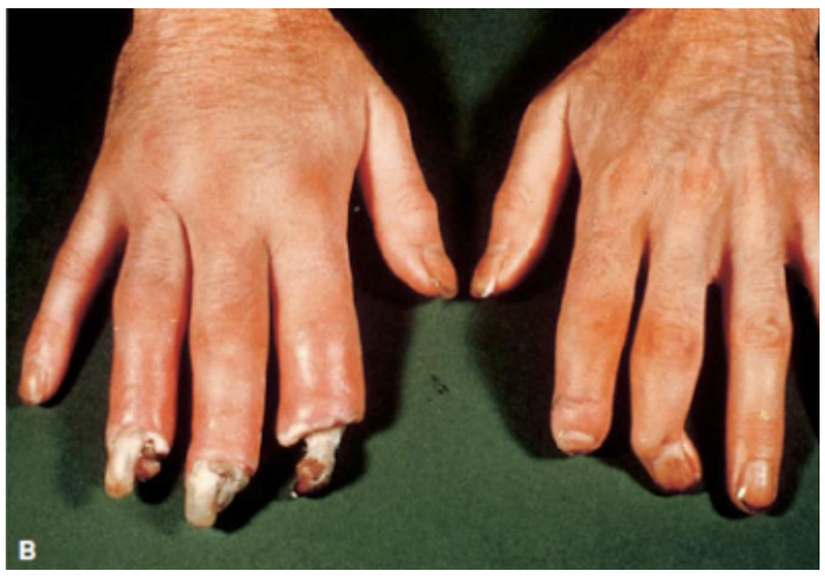
- Chronic **ulcerations** of the toes, or fingers may appear, followed in time by **gangrene**.

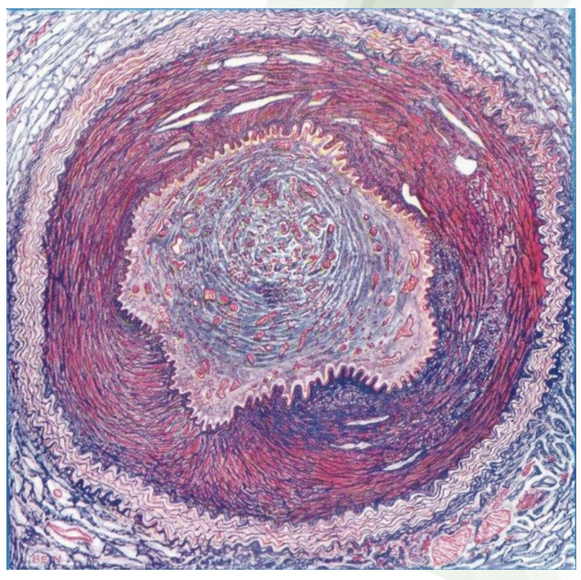


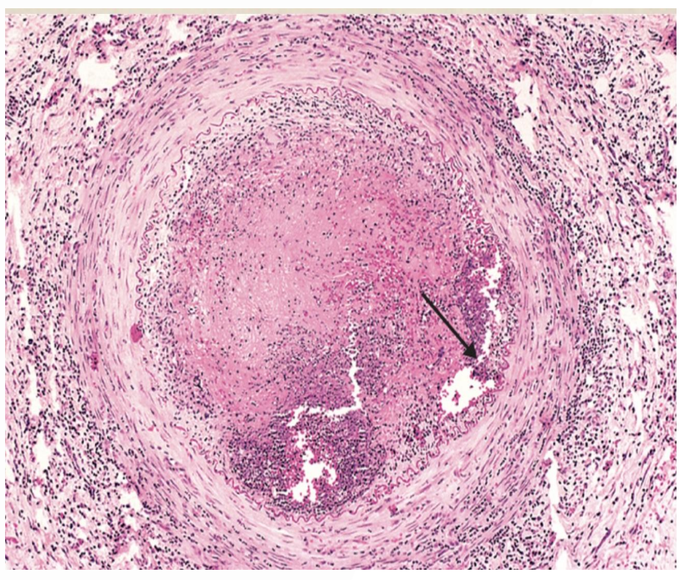
Morphology

- **Acute and chronic inflammation**,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.
- **luminal thrombosis**









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