

• ***Pathology of vascular system***

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Lecture 3&4

Inflammatory diseases of blood vessels (Vasculitis):

- Vasculitis is a general term for vessel wall inflammation with variable manifestations depending on the organ affected.
- Besides the findings referable to the specific tissues involved, the clinical manifestations typically include constitutional signs and symptoms associated with systemic inflammation, such as fever, myalgia, arthralgia, and malaise.
- Vasculitis can affect any vessels of any type in any organ.

Etiology of vasculitis:

The main pathogenic mechanisms of vasculitis are:

1. Infectious:

- Direct invasion of the vascular walls by microorganisms e.g. bacteria (e.g. Neisseria), Spirochetal (syphilis), fungi and viruses.

2. Immunologic:

- Systemic lupus erythematosus and rheumatoid arthritis.
- Drug-induced Vasculitis
- Kawasaki disease.

3. Unknown:

- Giant cell (temporal) arteritis

- **Giant cell (temporal) arteritis**
- **Takayasu arteritis**
- **Polyarteritis nodosa**

- **Kawasaki disease**

- **Henoch-Schonlein purpura**

- **Thromboangitis obliterans (Burger's disease)**

Giant cell (temporal) arteritis

It is a chronic, classically granulomatous inflammation of large- to small-sized arteries that principally affects arteries in the head.

It is the most common form of vasculitis among elderly adults over 50 yrs.

The temporal arteries, vertebral and ophthalmic arteries, as well as the aorta (giant cell aortitis), also can be involved.

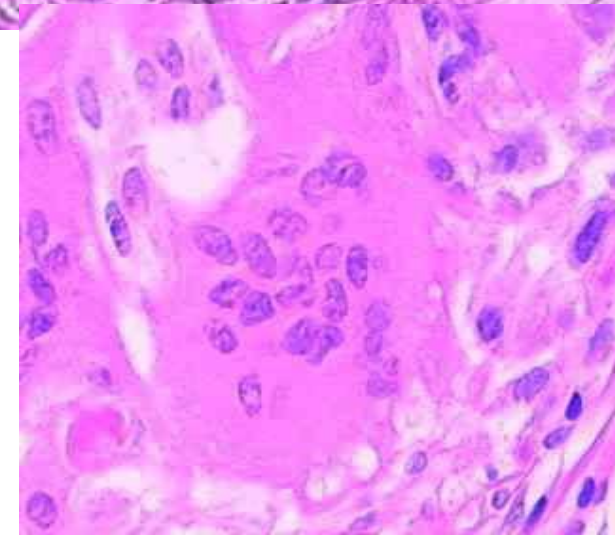
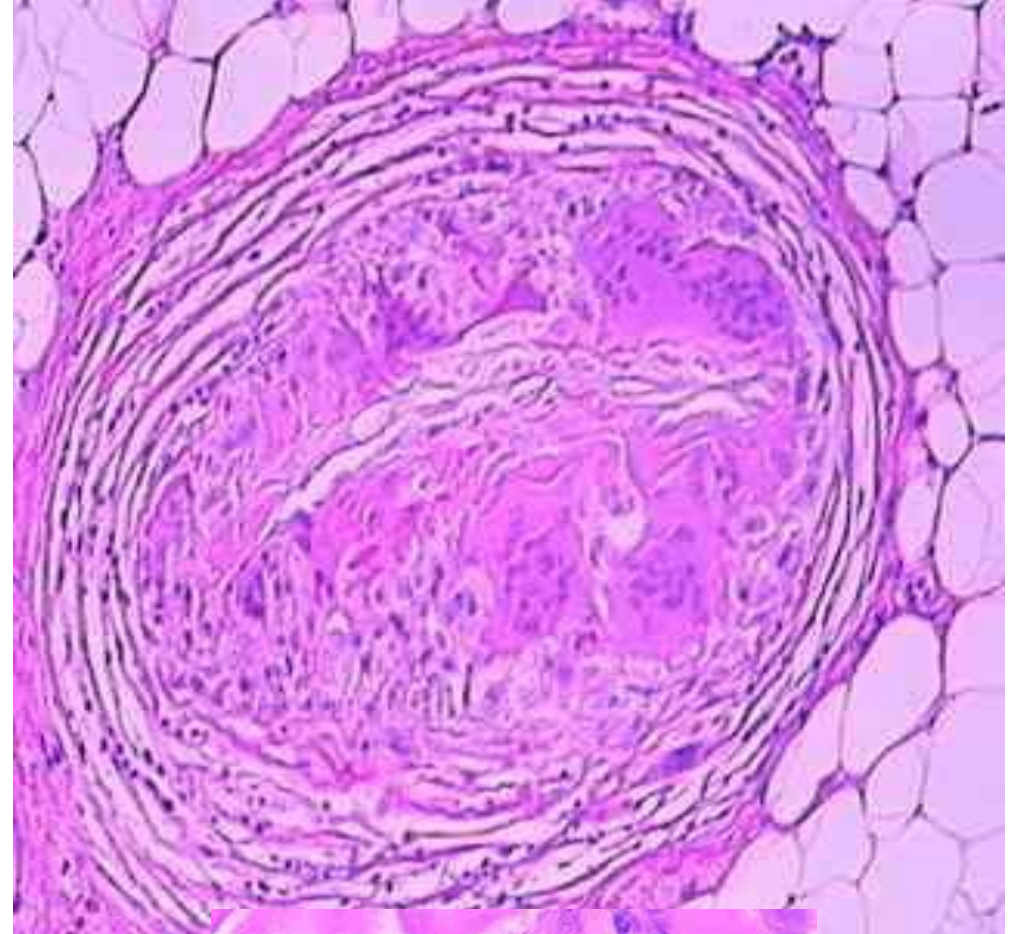
Because ophthalmic artery involvement can lead to sudden and permanent blindness, affected persons must be diagnosed and treated properly

• **Morphology of Giant cell Arteritis:**

- The commonest pattern characterized by:
 - Nodular thickenings of affected segment of arteries with reduction of the lumen and may become thrombosed.
 - Granulomatous inflammation of the inner half of the media
 - Fragmentation of the internal elastic lamina.

• Clinical Features

- Temporal arteritis is rare before age 50. Symptoms may be only constitutional: fever, fatigue or may involve facial pain or headache, most intense along the course of the superficial temporal artery, which can be painful to palpation.
- Ocular symptoms (associated with involvement of the ophthalmic artery) abruptly appear in about 50% of patients; these range from diplopia to complete vision loss.
- **Diagnosis** depends on biopsy and histologic confirmation, however, because giant cell arteritis can be focal within an artery, a negative biopsy result does not exclude the diagnosis.
- The ESR is often markedly elevated (over 100 mm/hr).
- **Corticosteroids or anti-TNF therapies are typically effective**



Giant cell arteritis The temporal artery of a patient with classic giant cell arteritis shows a thickened, nodular, and tender segment of a vessel on the surface of head (arrow)

• Takayasu Arteritis

- This is granulomatous vasculitis that classically involves the aortic arch.
- In half the cases, it affects also the pulmonary arteries.
- It is characterized principally by **ocular disturbances and marked weakening of the pulses in the upper extremities** (pulseless disease).
- It is seen predominantly in females younger than age 40.
- Autoimmune mechanisms are suspected.
- **Microscopically:** there is chronic inflammation of the adventitia and the media, sometimes with granulomatous inflammation.
- Thus, the disease may be indistinguishable from giant cell (temporal) arteritis.
- In fact, distinctions among giant cell lesions of the aorta are based largely on the age of the patient, and most giant cell lesions of the aorta in young patients are Takayasu arteritis.
- Involvement of the root of the aorta may cause dilation of the aortic valve ring, producing aortic valve insufficiency.

Polyarteritis nodosa

- PAN is a systemic vasculitis of small- or medium-sized muscular arteries that typically affects renal and visceral vessels but spares the pulmonary circulation.
- The cause remains unknown in the majority of cases.
- **Pathological features:**
- PAN is associated with segmental transmural necrotizing inflammation of small- to medium-sized arteries, often with superimposed aneurysms and/or thrombosis and fibrinoid necrosis.
- **Kidney, heart, liver, and gastrointestinal tract vessels are involved.**

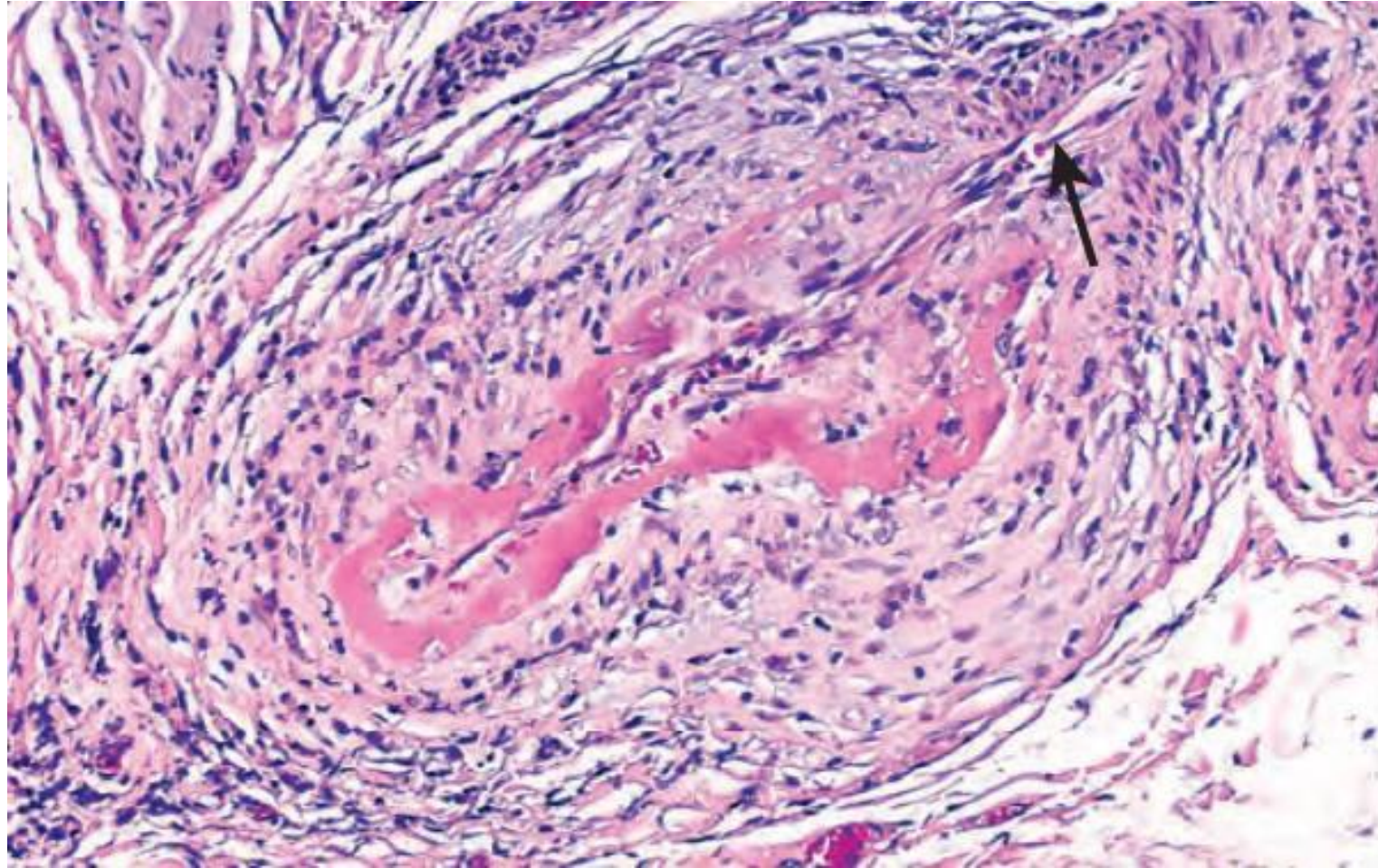
Clinical features:

PAN is primarily a disease of young adults but can occur in all age groups, the course is frequently remitting and episodic.

Typical presentation include rapidly accelerating hypertension due to renal artery involvement; abdominal pain and bloody stools caused by vascular gastrointestinal lesions

Renal involvement is often a major cause of mortality.

Untreated, PAN is typically fatal, but immunosuppression can result in remissions or cure in 90% of cases.



Polyarteritis nodosa :there is segmental fibrinoid necrosis and thrombotic occlusion of the lumen of this small artery. Note that part of the vessel wall at the upper right (arrow) is uninvolved

Kawasaki disease

This is an acute, febrile, usually self-limited illness of infancy and childhood associated with large- to medium- sized vessel arteritis.

80% of the patients are younger than 4 years of age.

Its clinical significance related to **involvement of coronary arteries** which can result in aneurysms that rupture or thrombose, causing MI and death.

In genetically susceptible persons, a variety of infectious agents (mostly viral) have been regard as triggering of this disease.

✓ **Clinical features: (Mucocutenous LN syndrome)**

1. High fever
2. Skin rash
3. Erythema of the conjunctiva, oral mucosa, palms and feet.
4. Cervical lymphadenopathy.
5. Vasculitis **characteristically involves the coronaries.**

- **Henoch-Schonlein purpura**

- It is a small vessel vasculitis most commonly seen in children.
- It is characterized by abdominal pain, acute arthritis, glomerulonephritis and nonthrombocytopenic purpura that is distributed over the extensor aspects of the limbs and buttocks.
- These skin lesions consist of subepidermal necrotizing vasculitis involving small blood vessels.
- Deposition of IgA is present in the glomeruli and affect small blood vessels

Typical symptoms and signs of Henoch-Schönlein purpura

Raised reddish-purple spots or bruised areas mainly on buttocks, legs, and feet. In some individuals, spots may appear on body trunk, arms, and hands.

Abdominal pain, nausea, vomiting, bloody diarrhea

Joint inflammation and pain

Foot and ankle edema (swelling)



Henoch-Schonlein purpura

Thromboangitis obliterans (Burger's disease) :

- ✓ **It** is a distinctive disease characterized by segmental vasculitis with thrombosis of medium sized and small arteries especially the tibial and radial arteries that often leads to vascular insufficiency, typically of the extremities.
- ✓ **It occurs almost exclusively in heavy cigarette smokers, usually before the age of 35**, the relationship to cigarette smoking is a consistent feature of this disease which explained by endothelial injury either directly or through hypersensitivity to some tobacco products.

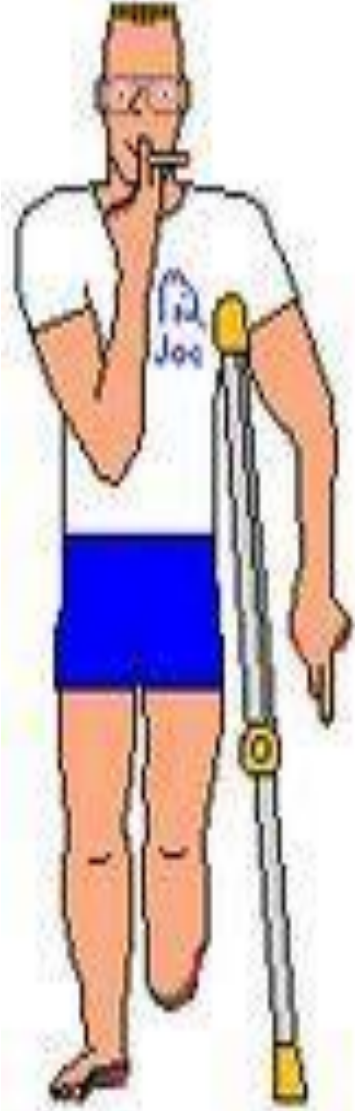
Morphology: Affected vessels show acute and chronic inflammation, accompanied by luminal thrombosis with small micro abscesses composed of neutrophils surrounded by granulomatous inflammation

Clinical features begin with features of vascular insufficiency e.g. pain on exercise and intermittent claudication.

Eventually gangrene of the extremities occurs that may be treated by amputation.

Remission and relapses correlate with cessation and resumption of smoking.

Buerger's Thromboangiitis Obliterans

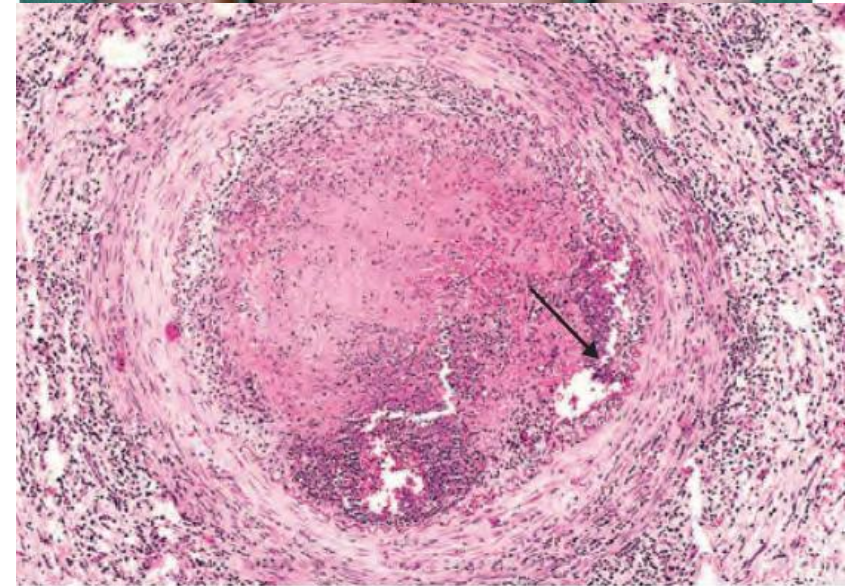
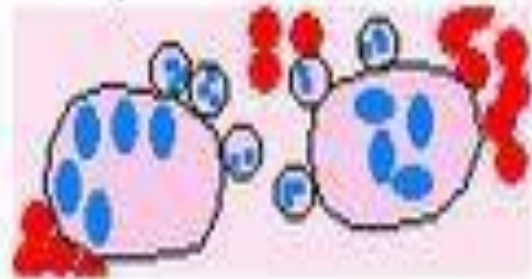


Pathologists look for:

1. Inflamed / scarred neurovascular bundles



2. Neutrophils adjacent to epithelioid giant cells deep inside thrombi



The lumen is occluded by a thrombus containing abscesses (arrow), and the vessel wall is infiltrated with leukocytes.

- **Raynaud's phenomenon**

- Raynaud phenomenon results from exaggerated vasoconstriction of arteries in responses to cold or emotion.
- It most commonly affects the extremities, particularly the fingers and toes, but also occasionally the nose, earlobes, or lips.
- The restricted blood flow induces paroxysmal pallor and even cyanosis in severe cases; involved digits classically show “red, white, and blue” color changes from most proximal to most distal, correlating with proximal vasodilation, central vasoconstriction, and more distal cyanosis
- Raynaud phenomenon may be a primary with no underlying cause or be secondary to a variety of conditions

- Primary Raynaud phenomenon

- Its affects 3% to 5% of the general population and shows a predilection for young women. Structural changes in the arterial walls are absent
- It tends to symmetrically affect the extremities
- The course of Raynaud phenomenon is usually **benign**, but when long-standing can result in atrophy of the skin, subcutaneous tissues, and muscles.
- Ulceration and ischemic gangrene are rare

- In contrast, secondary Raynaud phenomenon refers to vascular insufficiency of the extremities secondary to arterial disease including SLE, scleroderma, Burger disease, or even atherosclerosis.
- Clinically, secondary Raynaud phenomenon tends to have asymmetric involvement of the extremities and progressively worsens over time.
- The significance of Raynaud phenomenon is that it may be the first manifestation of immune-mediated vasculitis so any patient with new symptoms should be evaluated, of these patients 10% will manifest an underlying disorder.

Raynaud's Phenomenon



Vasoconstriction



Cyanosis



Vasodilation



Raynaud's phenomenon (A) Sharply demarcated pallor of the distal fingers resulting from the closure of digital arteries.
(B) Cyanosis of the fingertips.

- Varicose veins and phlebothrombosis/thrombophlebitis together account for at least 90% of clinical venous disease.
- **Varicose Veins**
- Varicose veins are abnormally dilated, tortuous veins produced by prolonged, increased intraluminal pressure with vessel dilation and incompetence of the venous valves.
- The superficial veins of the upper and lower leg are commonly involved because venous pressures in these sites can be markedly elevated (up to 10 times normal) by prolonged dependent posture.
- About 20% of men and a third of women develop lower extremity varicose veins, higher incidence in women probably reflects the prolonged elevation in venous pressure caused by compression of the inferior vena cava by the gravid uterus during pregnancy.

ischemia results from chronic venous congestion and poor vessel drainage leading to stasis dermatitis and ulcerations

Common varicosities in two other sites are :

Esophageal varices which occur commonly due to liver cirrhosis due to portal hypertension. Esophageal varices may rupture and lead to massive (even fatal) upper gastrointestinal hemorrhage.

Hemorrhoids can also result from primary varicose dilation of the venous plexus at the anorectal junction (e.g., through prolonged pelvic vascular congestion due to pregnancy or straining to defecate).

- **Thrombophlebitis and phlebothrombosis are largely interchangeable designations for venous thrombosis and inflammation involving deep leg veins in more than 90% of cases.**

- **Hemangiomas** are very common benign tumors characterized by increased numbers of normal or abnormal vessels filled with blood
- Common in infancy and childhood and constitute 7% of all
- benign tumors of infancy and childhood.
- The majority is superficial lesions, often of the head or neck, but they may occur internally, with nearly one third in the liver.
- Malignant transformation occurs rarely (if at all).
- There are several histologic and clinical variants
- 1- Capillary Hemangioma:
 - Juvenile hemangioma "strawberry type" of the skin of newborns is extremely common, and may be multiple.
 - It present from birth ,grows rapidly in the first few months, begins to fade when the child is 1 to 3 years old, and regresses by age 7 in 75% to 90% of cases.
 - **Gross:** bright red to blue lesion of the skin or slightly elevated.
 - **Mic:** aggregates of closely packed, thin-walled capillaries,
 - usually blood filled and lined by a flattened endothelium

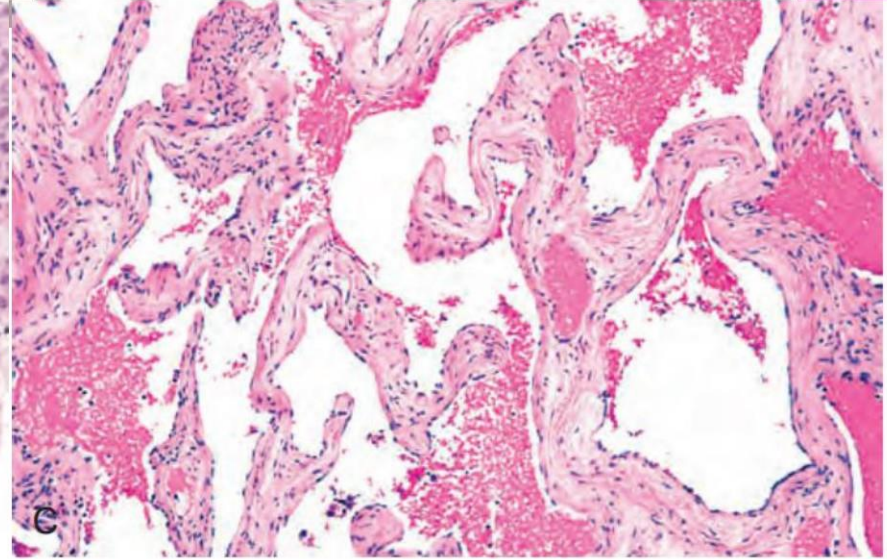
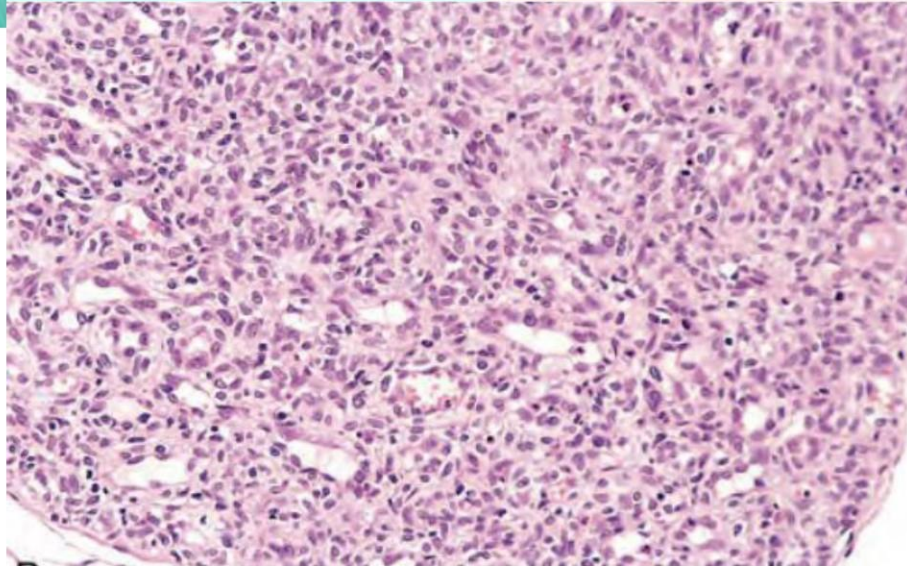
2 Cavernous hemangioma:

- Less common than the capillary hemangioma, characterized by the formation of large, dilated vascular channels, frequently involve deep structures (liver) .

3 Pyogenic granuloma

- It occurs in the gingiva of 1% of pregnant women and regresses after delivery.
- Red nodule attached by a stalk to the skin and gingival or oral mucosa, which bleeds easily and is often ulcerated.
- Approximately one third of lesions develop after trauma, resemblance to granulation tissue.
- The name of this lesion is misnomer it has no granuloma , not related to pyogenic infection

Hemangioma



Capillary hemangioma

Cavernous hemangioma

- **Intermediate-Grade (Borderline) Tumors Kaposi Sarcoma**

- Kaposi sarcoma (KS) is a vascular neoplasm caused by human herpesvirus 8 (HHV8, also known as Kaposi sarcoma herpesvirus). Although it occurs in a number of conditions, it is by far most common in patients with AIDS; also its presence is used as a criterion for diagnosis of AIDS.

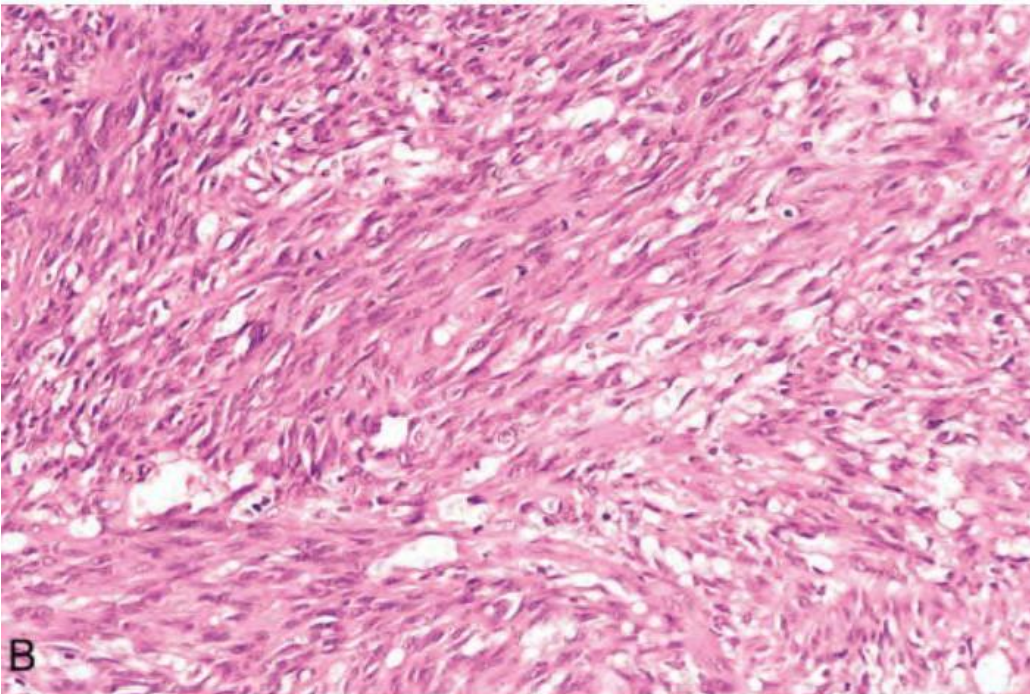
- Based on population demographics and risk factors,
- KS is categorized into four forms:
 - Classic KS is a disorder of older men of Mediterranean, Middle Eastern, or Eastern European descent; it is uncommon in the United States. It can be associated with malignancy or altered immunity, but it is not associated with human immunodeficiency virus (HIV) infection.
 - Endemic African KS typically occurs in HIV negative individuals younger than age 40 years and can follow an indolent or aggressive course.
 - Transplant-associated KS occurs in solid-organ transplant recipients receiving T-cell immunosuppression; the risk can be 100-fold greater than for immunocompetent patients.
 - AIDS-associated KS is an AIDS-defining illness, it represents the most common HIV-related malignancy.

- **Morphology:**

- Most common sites affected by kaposi sarcoma leg ,face, feet.
- In KS the cutaneous lesions progress through three stages: Patches ,then become larger and then become nodular .
- These lesions are composed of sheets of proliferating spindle cells, mostly in the dermis or subcutaneous tissues containing small vessels and slitlike spaces with red cells



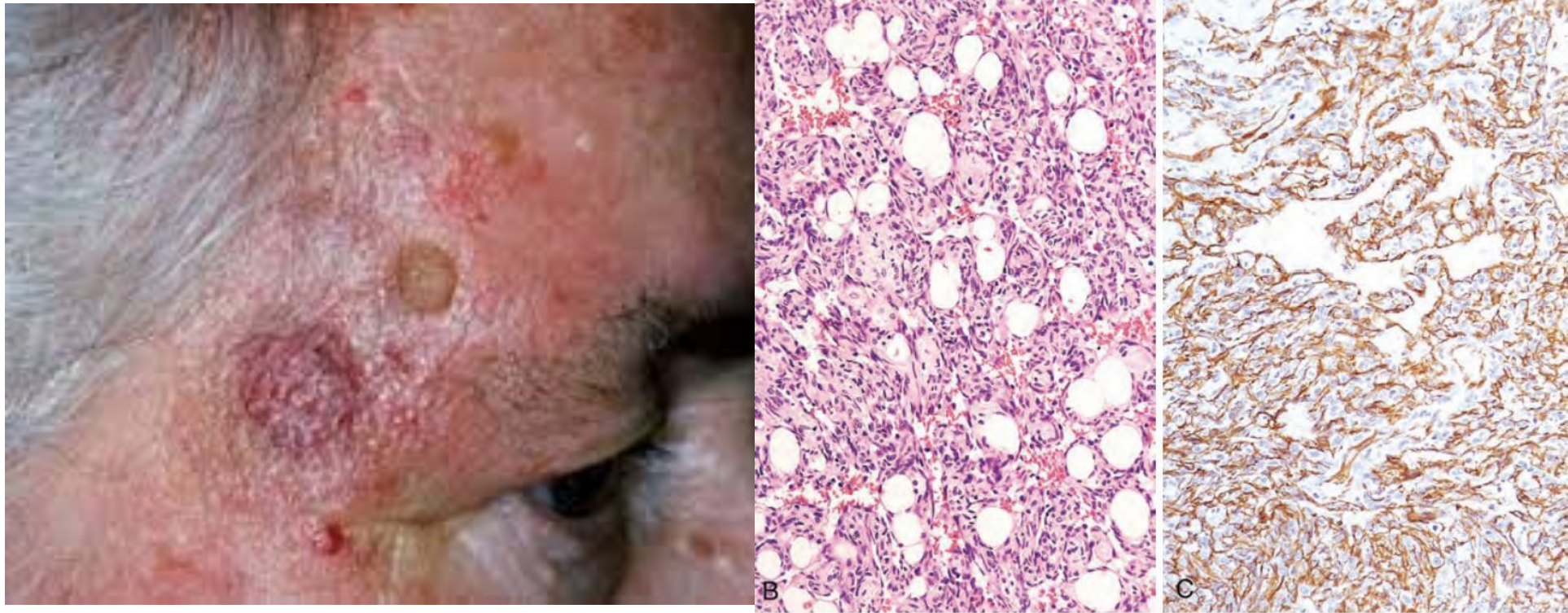
(A) Gross photograph show red purple macules and plaques of the skin.



(B) Histologic appearance of the nodular stage of Kaposi sarcoma, demonstrating sheets of plump, proliferating spindle cells.

- **Malignant Tumors (angiosarcoma).**

- Angiosarcomas are malignant endothelial neoplasms.
- They can be found anywhere in the body but most often in the skin, soft tissue, breast, and liver.
- They occur in both sexes and more often affect older adults.
- hepatic angiosarcomas are associated with distinct carcinogens, (arsenic, Thorotrast, and vinyl chloride).
- Gross: either small multiple red nodules; OR large, fleshy masses with central necrosis.
- Mic:, all degrees of differentiation of these tumors may present (from well differentiated angiosarcoma (hemangioma like), to anaplastic angiosarcoma .
- Immunohistochemical staining for the endothelial cell marker CD31 demonstrating the endothelial nature of the tumor cells and used to confirm the diagnosis.



A) Cutaneous angiosarcoma (B) Moderately differentiated angiosarcoma with dense clumps of atypical cells lining distinct vascular lumens. (C) Immunohistochemical staining for the endothelial cell marker CD31 demonstrating the endothelial nature of the tumor cells.