Blood Vessels

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Vascular Structure and Function

• All vessels except capillaries share a three-layered architecture consisting of an endothelium-lined intima, a surrounding smooth muscle media, and supportive adventitia, admixed with extracellular matrix (ECM).

• **Many disorders affect only particular types of vessels and therefore have characteristic anatomic distributions**.

• Atherosclerosis affects elastic and muscular arteries.
• Hypertension is a consequence of increased tone in small muscular arteries and arterioles.
• Different vasculitides characteristically affect only vessels of a certain caliber.
• Inflammatory cell exudation and increased permeability occur primarily at postcapillary venules.

Vascular Anomalies

Berry aneurysms are outpouchings in cerebral vessels due to congenital wall weakness; rupture can cause fatal intracerebral hemorrhage .

• **Arteriovenous fistulas** are abnormal communications between arteries and veins. They can be congenital or secondary to trauma, surgery, inflammation, or a healed ruptured aneurysm.

• **Fibromuscular dysplasia** is focal, irregular thickening and attenuation of the arterial wall due to intimal and medial hyperplasia and fibrosis.

Vascular Wall Response to Injury

Endothelial Cells functions:

- Maintenance of a permeability barrier
- Elaboration of prothrombotic, antithrombotic, and fibrinolytic mediators
- ECM production
- Modulation of blood flow and vasomotor tone
- Regulation of inflammation
- Regulation of cell growth

Blood Pressure Regulation

Blood pressure is the product of cardiac output and peripheral vascular resistance, which are in turn influenced by genetic and environmental factors .

• **Cardiac output** is determined by myocardial contractility, heart rate, and blood volume.

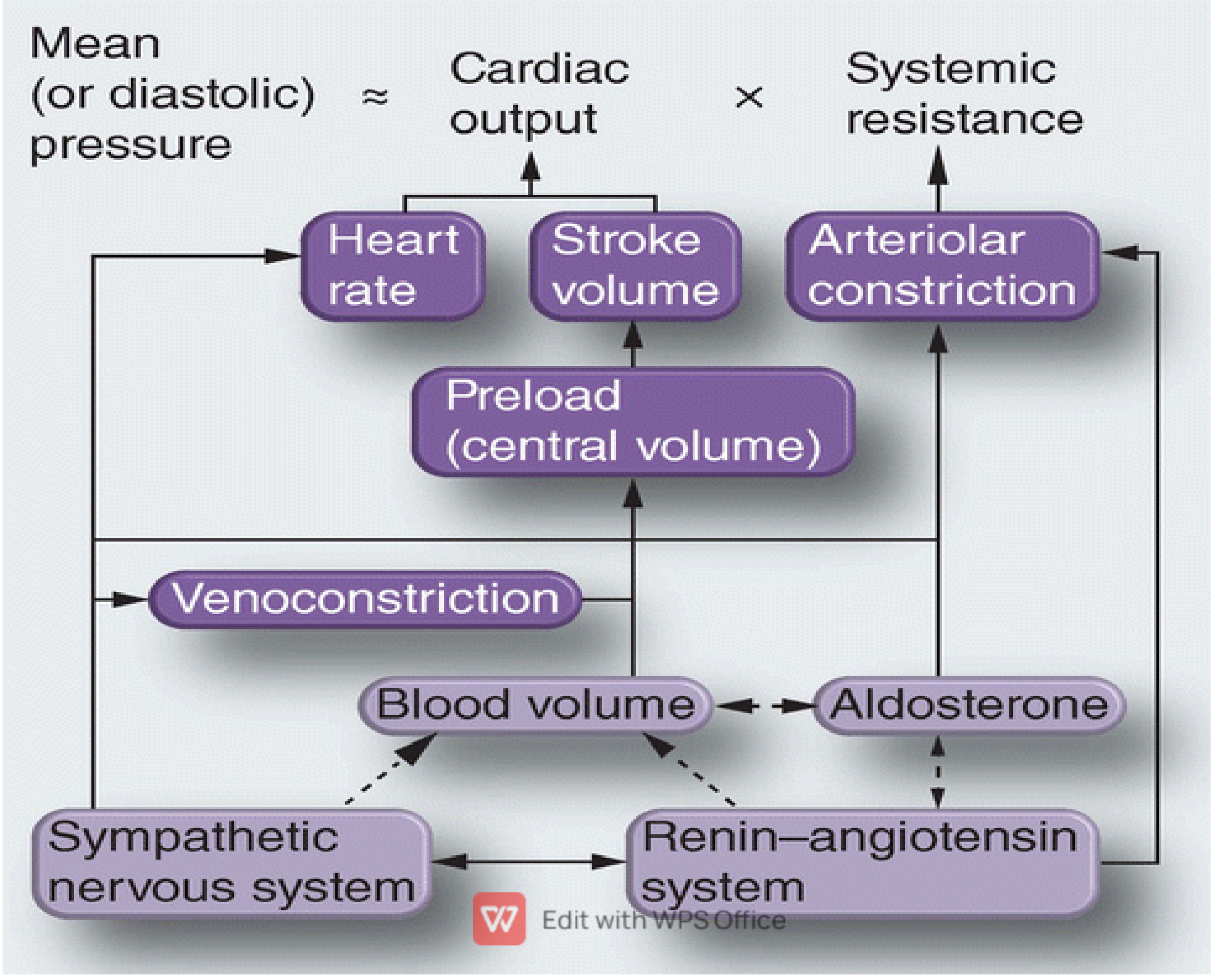
Blood volume is affected by the following:

• Sodium load
• Mineralocorticoids (aldosterone)
• Natriuretic peptides induce sodium excretion; these are produced by atrial and ventricular myocardium in response to volume expansion.

Peripheral resistance is determined primarily at the level of the arterioles.

- **Vasoconstrictors**: Angiotensin II, catecholamines....,
- **Vasodilators**: Kinins, prostaglandins, ...
- **Regional autoregulation** occurs when increased blood flow leads to local vasoconstriction; local hypoxia or acidosis can also cause vasodilation.

- Kidneys have a major influence on blood pressure by producing **renin** in the setting of hypotension:
- Renin converts angiotensinogen to angiotensin I, which is subsequently converted to angiotensin II.
- Angiotensin II causes vasoconstriction.
- Angiotensin II also increases blood volume by inducing aldosterone production that increases renal sodium resorption.



Types and Causes of Hypertension SSS

Essential Hypertension

Secondary Hypertension

Renal

Acute glomerulonephritis

Chronic renal disease

Polycystic disease

Renal artery stenosis

Renal artery fibromuscular dysplasia

Renal vasculitis

Renin-producing tumors

Endocrine

Adrenocortical hyperfunction (Cushing syndrome, primary aldosteronism, congenital adrenal hyperplasia, licorice ingestion)

Exogenous hormones (glucocorticoids, estrogen [including pregnancy induced and oral contraceptives], sympathomimetics, tyramine‐containing foods, and monoamine oxidase inhibitors)
Pheochromocytoma
Acromegaly
Hypothyroidism ,Hyperthyroidism
Pregnancy induced
Cardiovascular ,Coarctation of aorta
Increased intravascular volume ,Increased cardiac output
Rigidity of the aorta
Neurologic ,Psychogenic
Increased intracranial pressure
Sleep apnea ,Acute stress.

Mechanisms of Essential Hypertension

In 90% to 95% of cases, hypertension is idiopathic (essential hypertension) . This does not mean that there is no cause but rather that cumulative effects of nongenetic environmental factors (e.g., stress, salt intake) cause high blood pressure.

Arteriosclerosis

is arterial wall thickening and loss of elasticity; the following three patterns are recognized:

- **Arteriolosclerosis**, primarily affecting small- and medium-sized arteries .

- **Mönckeberg medial sclerosis,** characterized by medial calcification in muscular arteries .

- **Atherosclerosis**, the most frequent and clinically important .

Atherosclerosis

Atherosclerosis is a slowly progressive disease of large- to medium□sized muscular and elastic arteries.

The lesions are characterized by elevated intimal-based plaques **composed of:**
lipids, proliferating SMC, inflammatory cells, and increased ECM.

They cause pathology by the following:

- Mechanically obstructing flow, especially in smaller-bore vessels
- Plaque rupture leading to vessel thrombosis
- Weakening the underlying vessel wall, leading to aneurysm

1. Constitutional Risk Factors

• **Genetics**: Family history is the most significant independent risk factor for atherosclerosis. .

• **Age**: Atherosclerotic burden progressively increases with age,

Gender: premenopausal women are relatively protected against atherosclerosis and its complications. .

2. Modifiable Major Risk Factors

- **Hyperlipidemia and hypercholesterolemia:** Increased risk is associated with increased (LDL) and decreased (HDL,) Levels can be favorably modified by diet, exercise, moderate alcohol intake, and statins
- **Hypertension**: high blood pressure increases the risk of atherosclerotic ischemic heart disease by 60%.
- **Smoking**: Smoking of one pack of cigarettes daily over several years doubles the death rate from ischemic heart disease.
- **Diabetes mellitus:** diabetes accelerates atherosclerosis and doubles the risk of myocardial infarction, as well as markedly increasing the risk of stroke or extremity gangrene.

Pathogenesis of Atherosclerosis

1.Endothelial Injury

Even without the loss of EC, EC dysfunction will result in increased adhesivity and procoagulant activity; the vessel responds with intimal thickening; in the presence of circulating lipids, typical atheromas ensue .

2. Hemodynamic Disturbances

atherosclerotic plaques are not randomly distributed and in fact characteristically develop at areas of disturbed flow.

3. Inflammation

Dysfunctional ECs express increased levels of adhesion molecules (e.g., vascular cell adhesion molecule-1 [VCAM-1]), promoting increased inflammatory cell recruitment. Subsequent T-cell and macrophage accumulation and activation lead to local increased cytokine production that drives SMC proliferation and matrix synthesis.

4. Infection

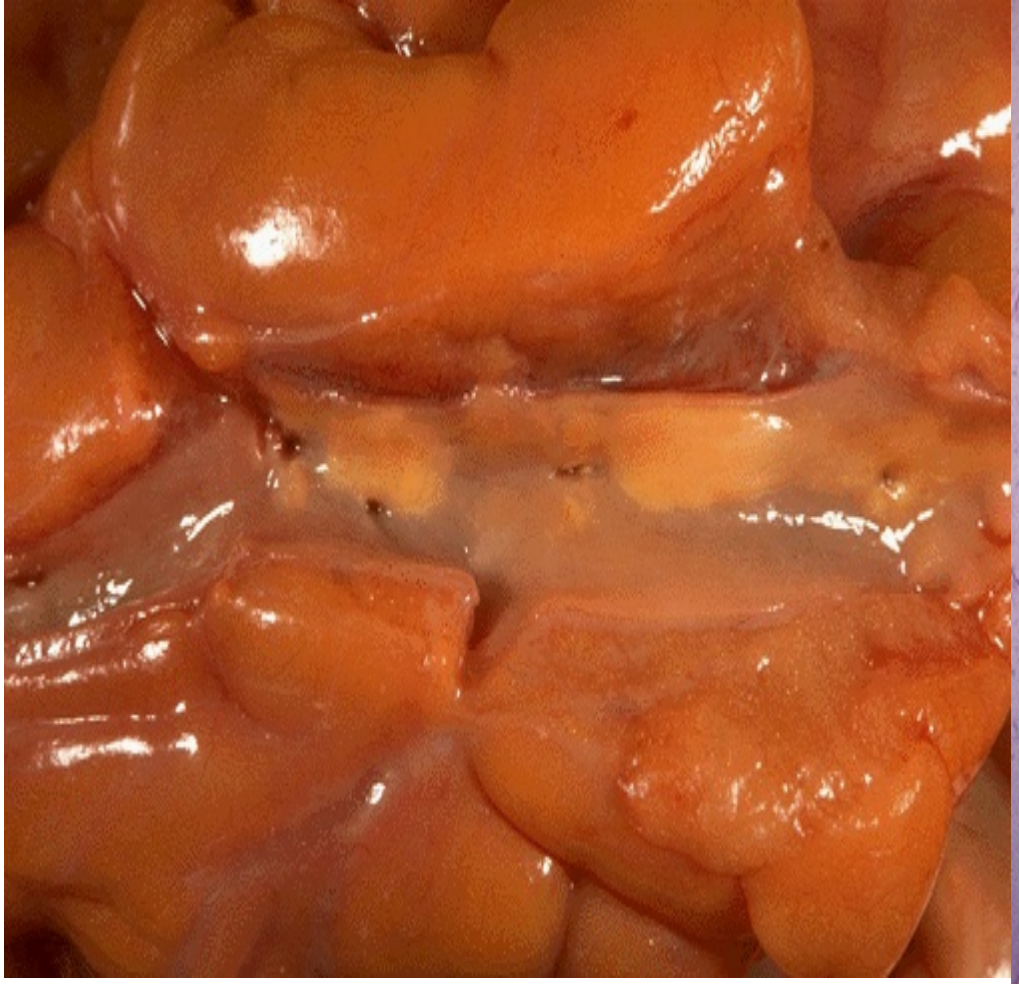
Herpesvirus, cytomegalovirus, and Chlamydia pneumoniae have all been detected in atherosclerotic plaques.

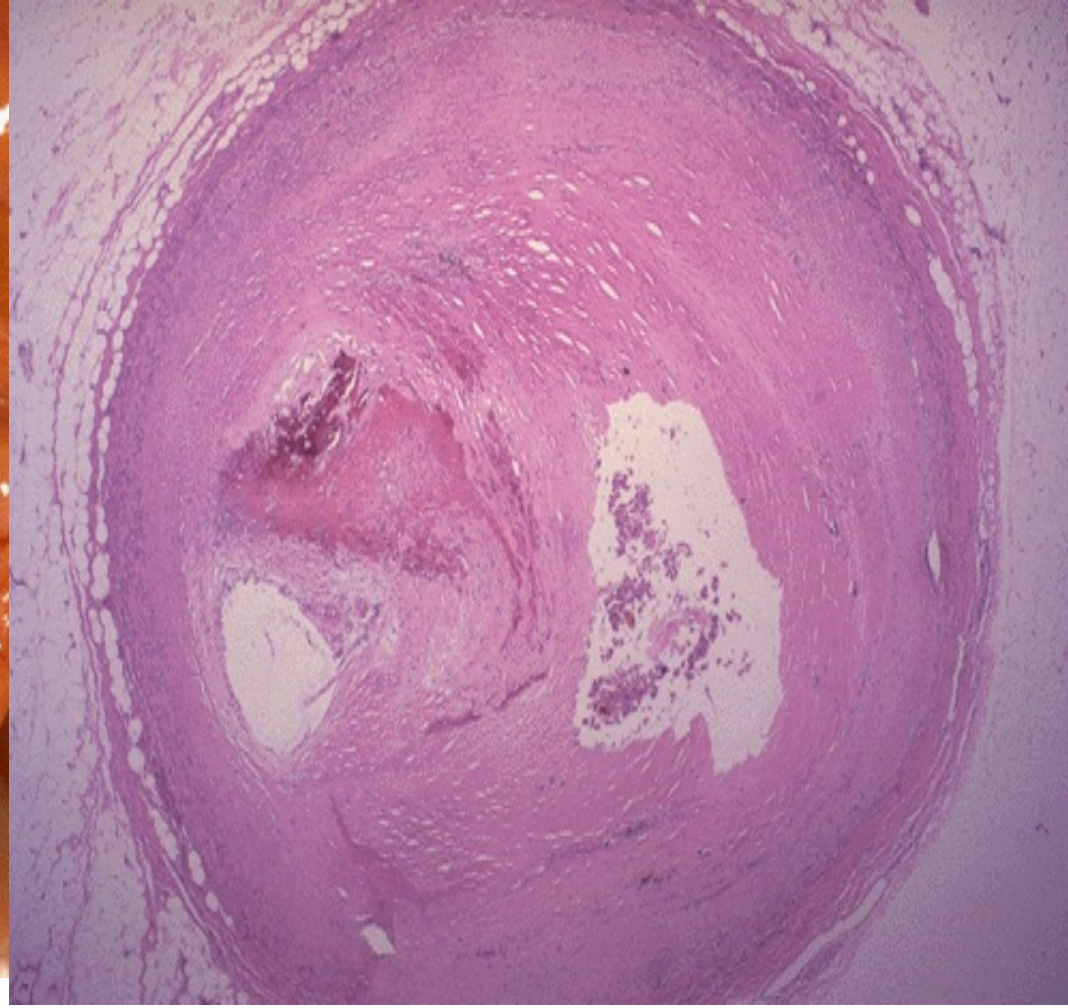
5. Smooth Muscle Proliferation and Matrix Synthesis through the activities of platelet-derived growth factor (released by adherent platelets and inflammatory cells), fibroblast growth factor, and transforming growth factor (TGF)-α.

Morphology

• **Fatty streaks** are early lesions composed of intimal collections of foamy macrophages and SMCs that gently protrude into the vascular lumen. These can occur at virtually *any age and even in infants* and occur at sites that often will eventually develop atherosclerotic plaques. Nevertheless, not all fatty streaks are destined to become atheromatous plaques.

• The characteristic atheromatous plaque (atheroma or fibrofatty plaque) is a raised, white-yellow, intimal-based lesion.





Mic. .Plaques are composed of superficial fibrous caps containing SMCs, inflammatory cells, and dense ECM overlying necrotic cores, containing dead cells, lipid, cholesterol foam cells, and plasma proteins; small blood vessels proliferate at the intimal-medial

Consequences of Atherosclerotic Disease

1.Atherosclerotic Stenosis

• At approximately 70% stenosis (critical stenosis), the vascular supply typically becomes inadequate to meet demand, and ischemia supervenes.

2. Acute Plaque Change

means that there is plaque erosion, rupture, or hemorrhag into the plaque (which expands the plaque volume and ca increase luminal stenosis).

3.Thrombosis

A thrombus that forms over atherosclerotic plaque can occlude the lumen

4. Vasoconstriction

Vasoconstriction can occur at sites of plaque formation due to endothelial dysfunction

5. Vessel Wall Weakening

Aneurysms and Dissection

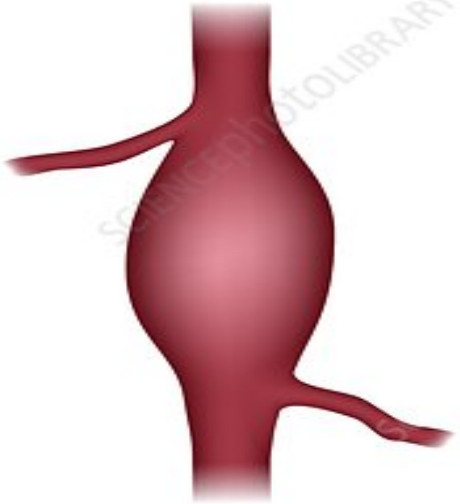
Aneurysms are abnormal vascular dilations.

A true aneurysm is bounded by all three vessel wall layers (intima, media, and adventitia),

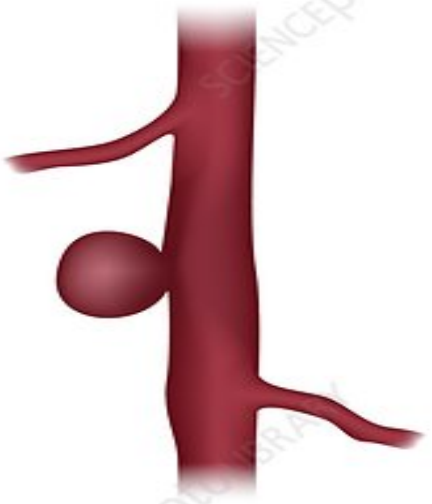
a false aneurysm is an extravascular hematoma that communicates with the intravascular space;

A dissection occurs when blood enters the arterial wall itself, dissecting between the layers.

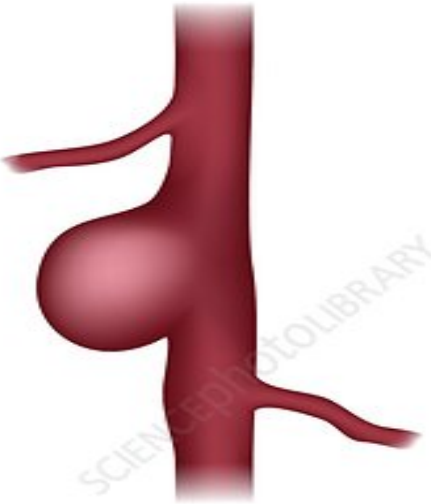
Types of aneurysm



fusiform



pseudoaneurysm



saccular

dissecting

ruptured

Pathogenesis of Aneurysms

Aneurysms occur due to the following:

- **Poor intrinsic quality of the vessel matrix**: In Marfan syndrome ,Ehlers-Danlos syndrome ,vitamin C deficiency

Imbalance of matrix synthesis and degradation: in atherosclerotic plaque or in vasculitis

- **Loss of medial SMCs or change in SMC synthesis:** Ischemia , dilation.

The most common causes of aneurysms are

- **atherosclerosis**
- **hypertension**.
- **syphilis,**
- **trauma,**
- **vasculitis,**
- **congenital defects** (e.g., berry aneurysms).
- **infections** (mycotic aneurysms) can originate from sep
  embolization (e.g., from bacterial endocarditis),

Cx:

- Rupture
- Impingement on adjacent structures
- Occlusion of proximal vessels by extrinsic pressure or superimposed thrombosis
- Embolism from a mural thrombus

Vasculitis

Vasculitis is vessel wall inflammation;

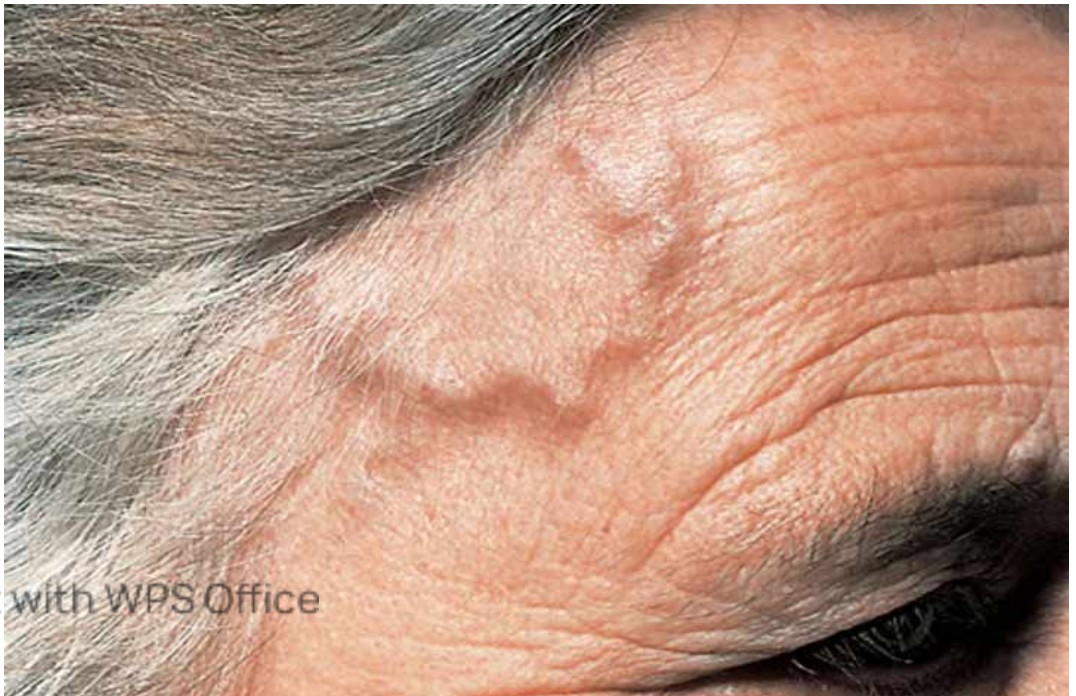
symptoms are typically referable to the ischemia that occurs in the downstream tissues (due to vessel injury andthrombosis), as well as constitutional manifestations, such as fever, myalgias, arthralgias, and malaise.

The two most common **pathogenic mechanisms** are **immune-mediated inflammation** and **infections**; **physical and chemical injury (irradiation, trauma, toxins, etc.)** can also be causal.

Giant Cell (Temporal) Arteritis

common , elderly population; it is characterized by focal granulomatous inflammation of medium- and small-sized arteries, (most commonly the temporal arteries). The primary etiology is likely a T cell–mediated immune response to vessel wall antigen

presents with headache and facial pain; approximately 50% of patients and can cause permanent blindness. The disease responds well to steroids



Polyarteritis Nodosa

PAN is a systemic disease characterized by necrotizing vasculitis involving small-to-medium arteries; kidney, heart, liver, and gastrointestinal (GI) tract are involved in descending order, and the pulmonary circulation is spared. the etiology is unknown. PAN is largely a disease of young adults, with nonspecific systemic symptoms (fever, malaise, weight loss) and clinical presentations related to the tissues involved (e.g., hematuria, albuminuria, and hypertension [kidneys]).

Kawasaki Disease

self-limited illness of infants and children associated with a medium-large vessel arteritis. The etiology is a T cell hypersensitivity to yet unidentified antigens.
the disease is typically heralded by fever lymphadenopathy, skin rash, and oral or conjunctival erythema.

Behçet Disease

a small- to medium-vessel neutrophilic vasculitis, typically presenting as a triad of the following:

- Recurrent oral aphthous ulcers
- Genital ulcers
- Uveitis

Granulomatosis With Polyangiitis (Wegener Granulomatosis)

is a necrotizing vasculitis associated with a triad of the following:

- Necrotizing or granulomatous vasculitis of small-to-medium vessels mostly in the lung and upper airway
- Necrotizing granulomas of the upper and lower respiratory tract
- Glomerulonephritis

Infectious Vasculitis

Arteritis can be caused by direct invasion from an adjacent source (especially Aspergillus and Mucor) or originate from septic embolization (e.g., from bacterial endocarditis).

Raynaud Phenomenon

Raynaud phenomenon results from exaggerated vasoconstriction of digital arteries and arterioles, producing pain, pallor, and even cyanosis; prolonged vasospasm can result in tissue necrosis.

- most commonly affects young women; it reflects exaggerated vasomotor responses to cold or emotion. The clinical course is usually benign.

Varicose Veins

These are typically superficial lower extremity veins that are dilated and tortuous due to chronically elevated intraluminal pressure.

Causes :

obesity

pregnancy .

hereditary venous defects

prolonged dependent leg position.

Esophageal varices are typically due to portal vein hypertension

Hemorrhoids can also result from primary dilation of the anorectal venous plexus (e.g., secondary to pregnancy or chronic constipation).

Thrombophlebitis and Phlebothrombosis

These are largely interchangeable terms for venous thrombosis and inflammation.

Predisposing factors for deep vein thrombosis (DVT)
congestive heart failure,
prolonged immobilization,
local infection, or
systemic hypercoagulability (e.g., neoplasia, pregnancy, or the postoperative state).

DVT are common sources of pulmonary emboli.

Lymphangitis and Lymphedema

Lymphangitis denotes the inflammation occurring when infections spread into lymphatics; β-hemolytic streptococ are a common cause. Lymphangitis presents as painful subcutaneous red streaks, often with tender regional lymphadenopathy (lymphadenitis).

Lymphedema is due to lymphatic obstruction and dilation, with associated increases in interstitial fluid.

Primary hereditary causes include Milroy disease (primary lymphatic agenesis). Common

secondary causes of lymphedema are as follows:

- Malignancy
- Surgical resection of regional lymph nodes
- Postradiation fibrosis
- Filariasis
- Postinflammatory thrombosis with lymphatic scarring

Vascular Tumors

Benign tumors

Hemangiomas

• **Capillary hemangiomas** are the most common type of vascular tumor, occurring primarily in skin or mucous membranes. These are unencapsulated lesions composed of closely packed aggregates ofcapillary-sized thin-walled vessels.

• **Cavernous hemangiomas** are unencapsulated lesions exhibiting large, thin-walled vascular spaces. In addition to the skin,the liver is a common site.

• **Pyogenic granulomas** polypoid Capillary hemangiomas

Lymphangiomas

Lymphangiomas are the benign lymphatic analog of hemangiomas

Intermediate-Grade (Borderline) Tumors

Kaposi Sarcoma

Kaposi sarcoma (KS) is a vascular neoplasm caused by human herpesvirus 8 (HHV-8),

KS is categorized into the following four varieties:

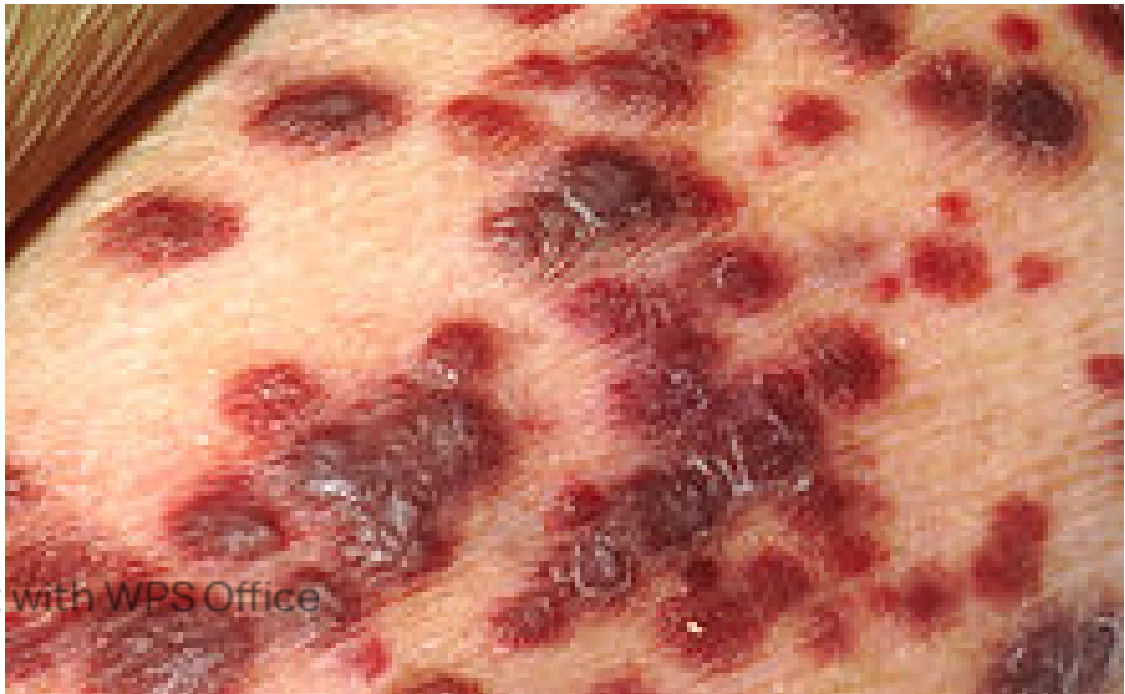
- **classic KS** occurs typically in elderly men of

it is not associated with (HIV). Lesions are red-purple cutaneous plaques and nodules on the lower extremities

- **endemic KS** it typically occurs in individuals younger than age 40 and is not associated with HIV. occurs largely in lymph node

Transplant-associated KS occurs in patients receiving chronic immunosuppression.

- **Acquired immunodeficiency syndrome (AIDS)–associated (epidemic) KS**



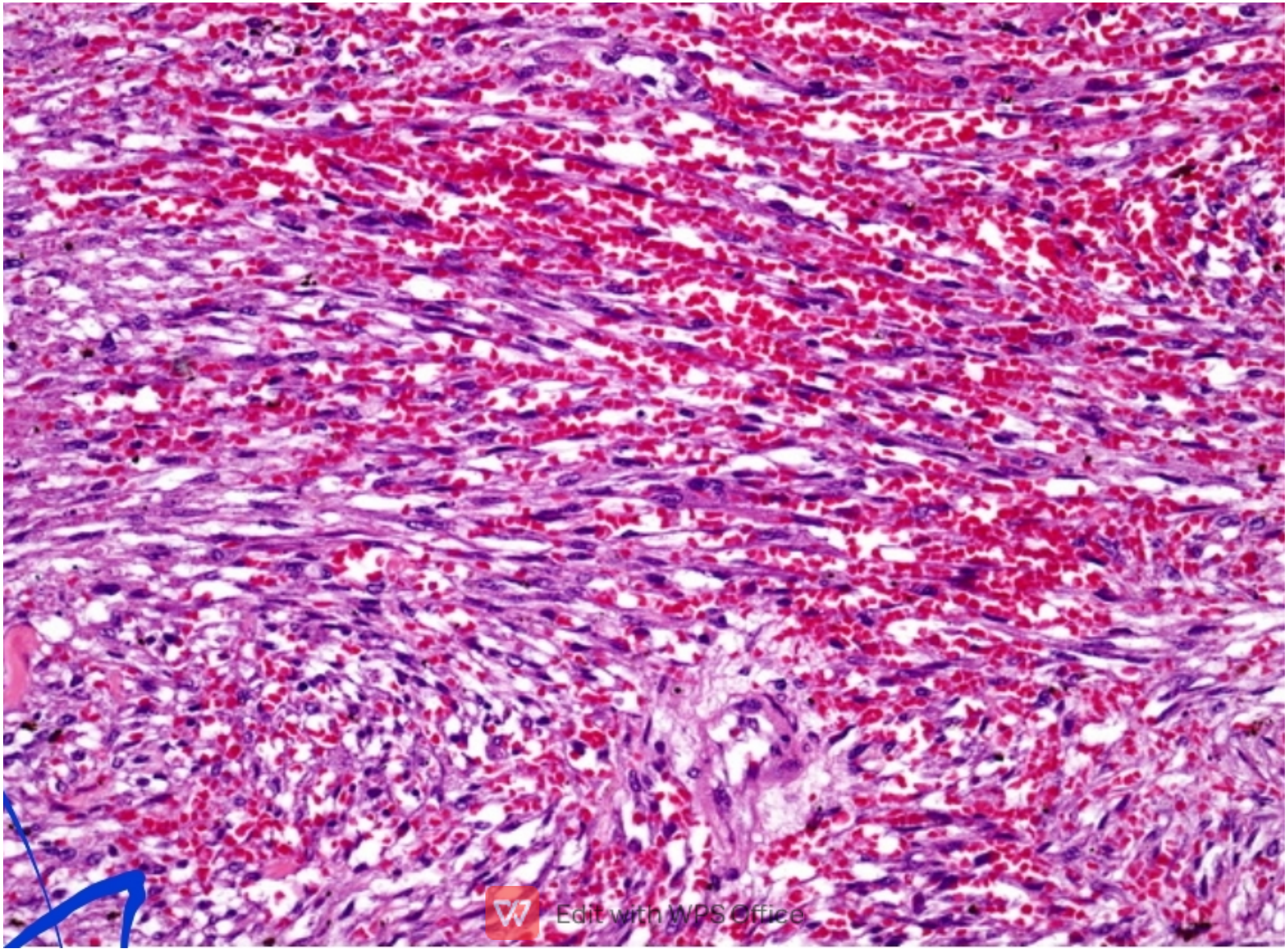
Three stages of lesions are recognized as the following:

• **Patches** are pink-purple macules, usually confined to the distal lower extremities.

• **Raised plaques** have dilated, jagged vascular channels lined by plump spindle cells accompanied by perivascular aggregates of similar spindled cells.

• **Nodular lesions** are more distinctly neoplastic

Microscopically lesions consist of
sheets of plump, spindle-shaped cells creating slitlike vascular spaces filled with erythrocytes; there are intermingled small vessels, with marked hemorrhage and mononuclear inflammatory cell infiltration



Malignant Tumors

Angiosarcomas

Angiosarcomas are malignant endothelial neoplasms on a spectrum from well-differentiated to anaplastic; they can occur anywhere but tend to arise in skin, soft tissue, breast, and liver.

risk factors

1.exposure to arsenic (some pesticides),
2.polyvinylchloride (some plastics),
3.Thorotrast (a radiocontrast agent no longer used).
4.long-termchronic lymphedema after radical mastectomy for breast cancer;
5.radiation and foreign bodies