Hemodynamic Disorders Thrombosis & Shock

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Circulatory disorders:

- Edema
- Hyperemia and Congestion
- Hemorrhage
- Thrombosis
- Embolism
- Infarction
- Shock

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Distribution of Body Water

- **Total body water:**
  - Varies from 45-75% of body weight
  - Young, healthy men = 50-60%
  - Young, healthy women = 45-50%
  - decreases with age

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Distribution of Body Water

- **Intracellular compartment:**
  - 2/3 of body water (**40% body weight**)
- **Extracellular compartment:**
  - 1/3 of body water (**20% body weight**)
    - **Plasma** (water = 4% - 5% body weight)
    - **Interstitial fluid** (water = 15% body weight)

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Edema: Normal fluid balance:

- 60% of body weight is water
- 2/3 (67%) of this fluid is intracellular
- 1/3 (33%) is extracellular, mostly as interstitial fluid
- ~ 5% of total body fluid is in the vascular compartment
- Fluid in 70 Kg man?

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Distribution of Body Water

- **In a healthy 70 kg male:**
- Total body water is ~ **42 L** ~ 60% BW
- **This is contained in two major compartments:**

1. the intracellular fluid (**28 L** ~ 40% BW)
2. the extracellular fluid (**14 L** ~ 20% BW)
   - the interstitial fluid (**10.5 L**, ~ 15% BW)
   - plasma (**3.5 L**, ~ 5% BW) ? Arterial ? Venous

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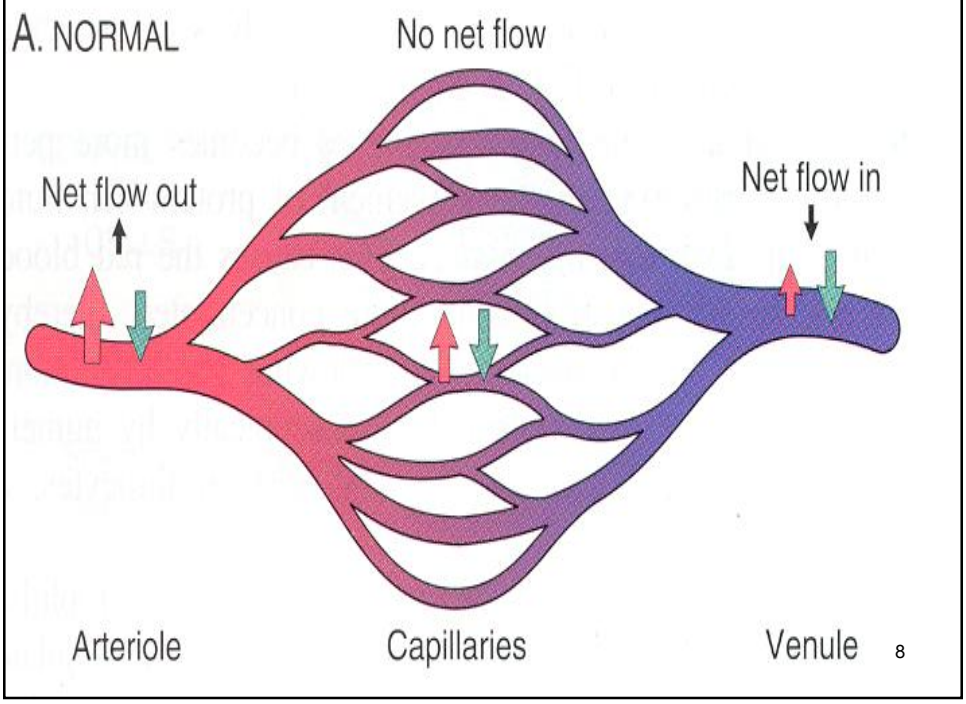
Normal fluid balance:

- The balance between **vascular hydrostatic pressure** and **plasma colloid osmotic pressure** is the driving force that maintains movement of fluids between vascular and interstitial spaces
- Normally, the exit of fluid into the interstitium at **the arteriolar end** is almost balanced by inflow of fluid from the interstitium back into the vascular bed at **the venular end**
- A small amount of fluid stays in the interstitium because of little higher hydrostatic pressure to push fluids out
- This little amount of fluid is drained back by **lymphatics** 7



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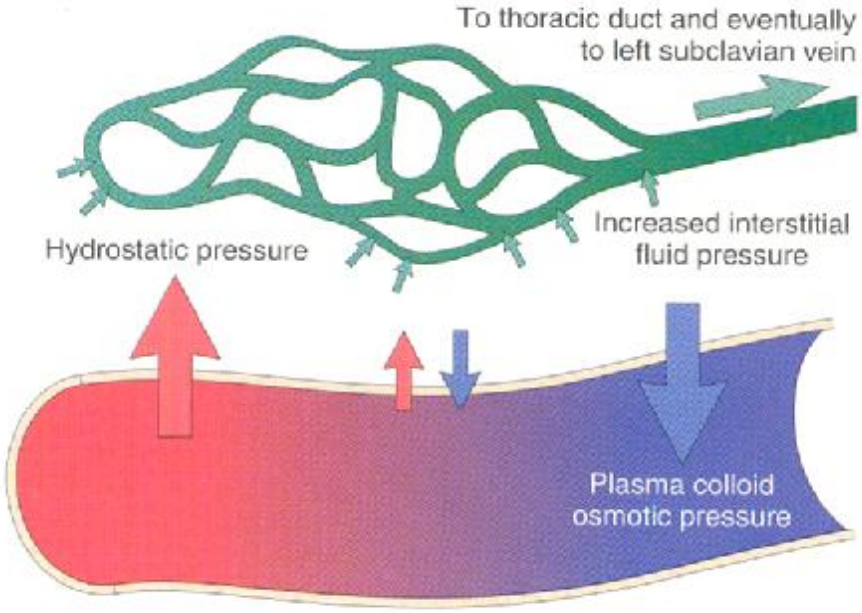
Normal fluid balance:



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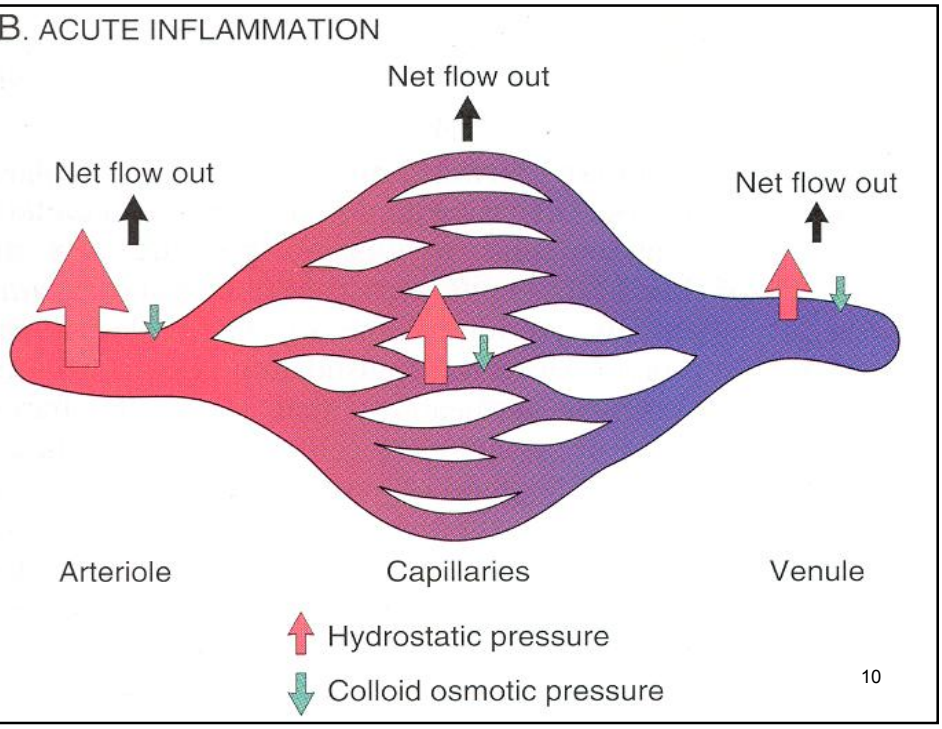

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Edema:

- **Edema** is **increased fluid in the interstitial tissue spaces**
- Collection of fluid in body cavities is named according to place:
  - **hydrothorax-** pleural effusion
  - **hydropericardium-** pericardial effusion
  - **hydroperitonium-** ascites
- **Anasarca** is severe and generalized edema with profound subcutaneous tissue swelling

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Edema mechanism:

- **Increased capillary hydrostatic pressure**
  - **Venous obstructions**
  - **Cardiac failure**
- **Decreased Osmotic pressure**
  - **Hypoproteinemia: liver disease**
- **Lymphatic obstruction**
  - **Elephantiasis**
- **Sodium Retention**
  - **Excessive salt intake with renal insufficiency**
- **Leaky vessels**
  - **Inflammation**

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Pathophysiologic Categories of Edema

Increased hydrostatic pressure:

I-Impaired venous return:

1- Congestive heart failure
2- Constrictive pericarditis
3- Ascites (liver cirrhosis)
4- Venous obstruction or compression:
   a- Thrombosis
   b- External pressure (tumor)
   c- Inactivity of lower limb

II- Arteriolar dilation:

1- Heat
2- Neurohumoral disturbance
3- Inflammation

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Pathophysiologic Categories of Edema

Reduced plasma osmotic pressure:

1- Protein losing glomerulopathies (nephrotic syndrome)
2- Liver cirrhosis
3- Malnutrition
4- Protein losing gastroenteropathy

Lymphatic obstruction:

1-Inflammatory
2- Neoplastic
3- Post-surgical
4- Post-irradiation

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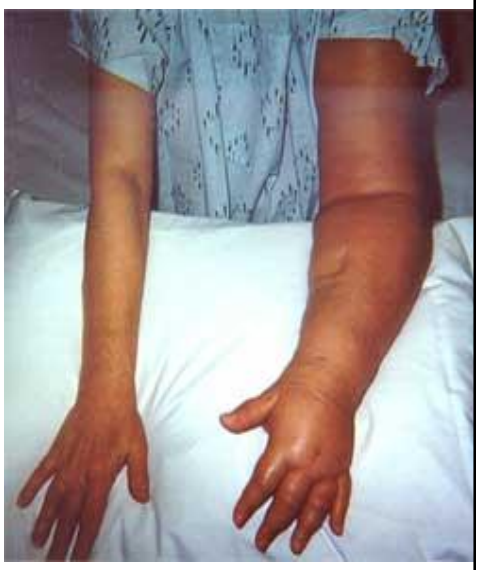
Lymphatic obstruction:

Lymphedema in the arm after left mastectomy



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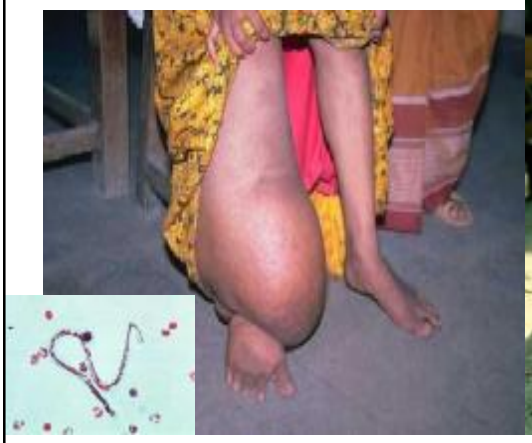
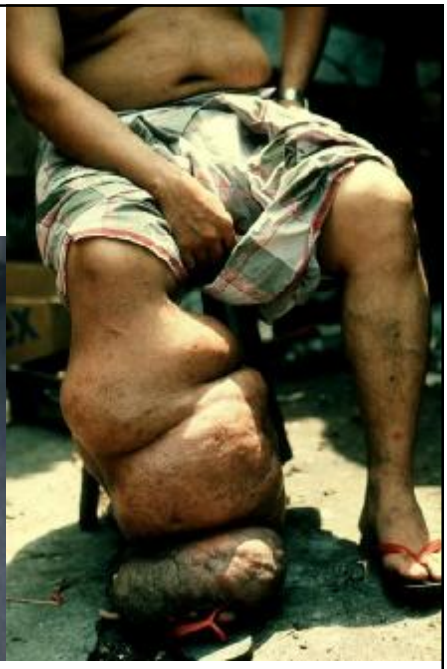
Lymphatic obstruction:





Elephantiasis: a case of filariasis

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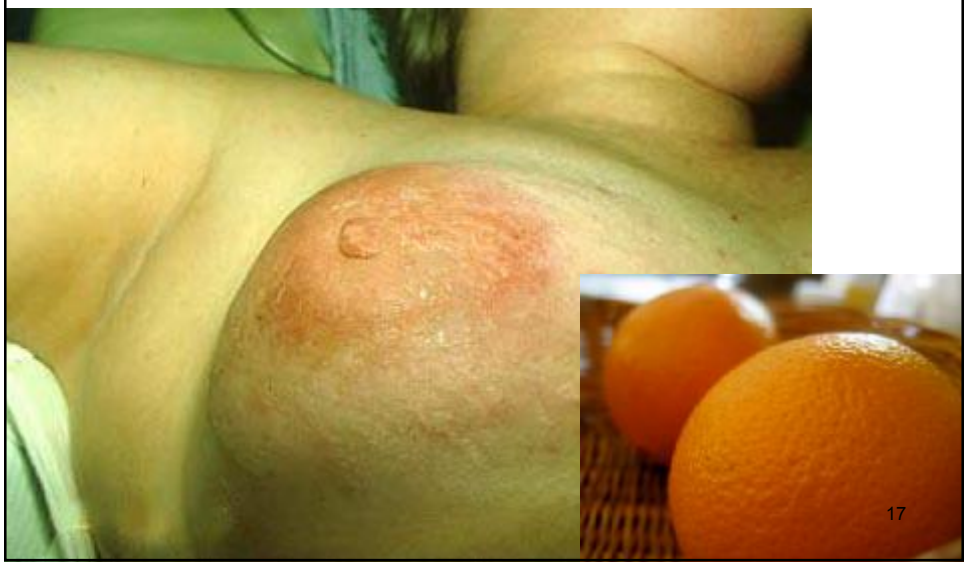
peau d'orange (orange peel) appearance



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Pathophysiologic Categories of Edema

Sodium retention:

1- Excessive Na intake with renal insufficiency

2- Increased tubular absorption of Na

a- **Renal hypoperfusion**

b- **Increased renin-angiotensin-aldosterone secretion**

Inflammation:

1- Acute inflammation

2- Chronic inflammation

3- Angiogenesis

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Subcutaneous edema

- Have different distributions depending on the cause
- It can be diffuse, or it may be more prominent in the regions with the highest hydrostatic pressures (the edema distribution is influenced by gravity and is termed **dependent**).
- **Edema of the dependent parts of the body** (e.g., the legs when standing) **is a prominent feature of cardiac failure, particularly of the right ventricle.**
- Finger pressure over significantly edematous subcutaneous tissue displaces the interstitial fluid and leaves **a finger-shaped depression**, so-called **pitting edema.**

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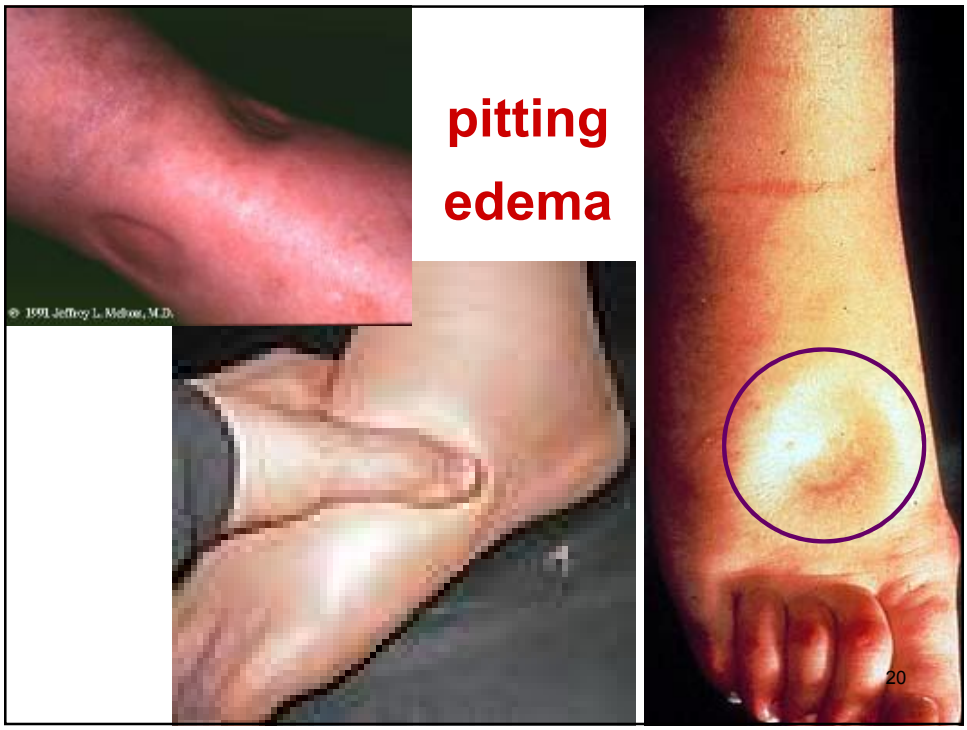

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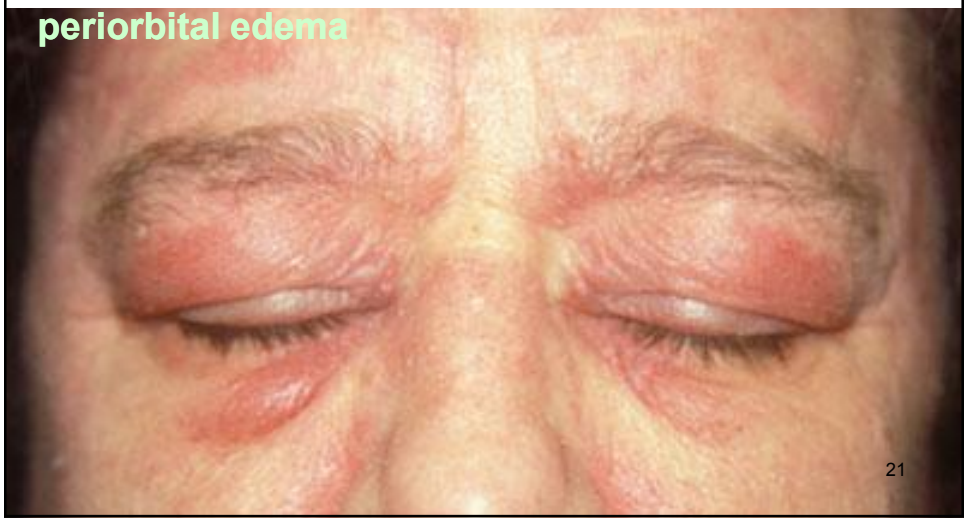
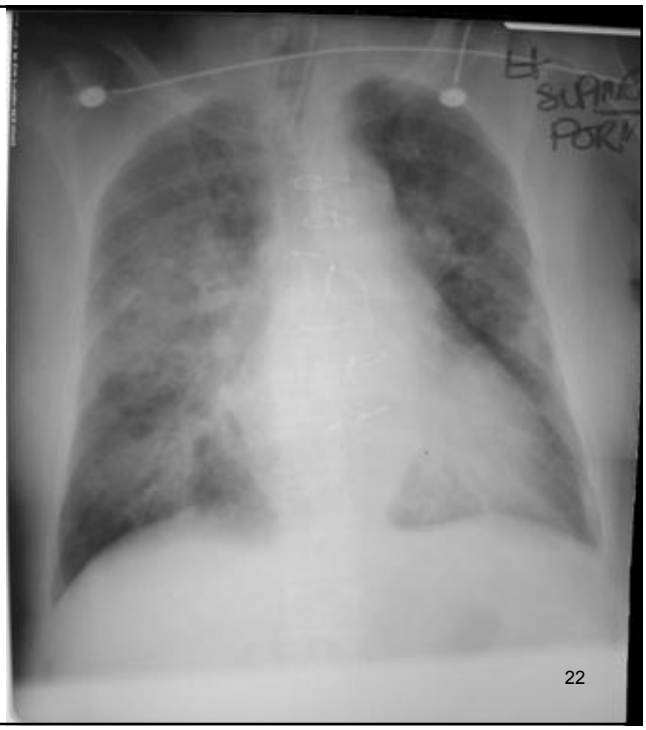
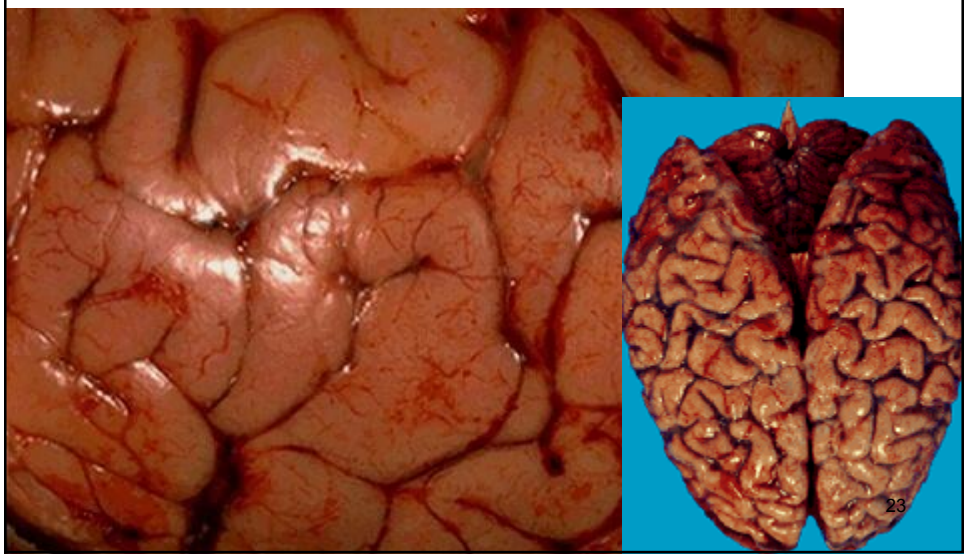
Edema due to **renal dysfunction or nephrotic syndrome** is more severe than cardiac edema **and affects all parts of the body equally.** It may be initially manifested in tissues with a loose connective tissue matrix, e.g. eyelids, causing **periorbital edema**



Pulmonary edema results in diffuse opacification of the lung



The surface of the brain with **cerebral edema** demonstrates widened gyri with a flattened surface. The sulci are narrowed.



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Name the two types of edema fluid:

Excudate:

Inflammatory edema has a high protein content and is associated with an inflammatory reaction.

Transudate:

Noninflammatory edema has a low protein content is caused by alterations in hemodynamic forces across the capillary wall (hemodynamic edema).

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Hyperemia and Congestion

Hyperemia:

- It's an **active** process that results from increased blood flow because of **arteriolar dilation**.
- Tissues that have hyperemia means that they **have more oxygenated blood** and will **appear more red**

Congestion:

- It's a **passive** process, it may result from **impaired venous return** from the tissue involved
- Tissues will **have deoxygenated blood**
- The tissue has a **blue-red** color (**cyanosis**)
- Causes may be local or systemic: cardiac or hepatic

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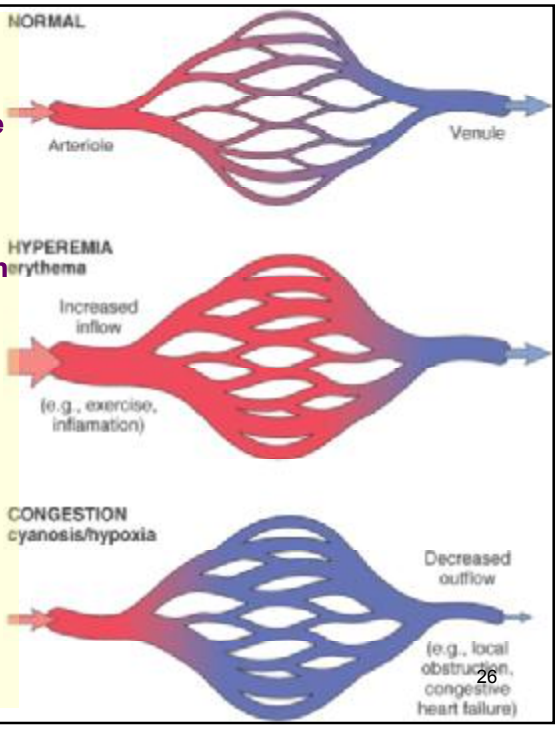
Hyperemia versus congestion:
In both cases there is an **increased volume and pressure** of blood in a given tissue with associated **capillary dilation** and a potential for **fluid extravasation**
In **hyperemia**, increased inflow leads to engorgement with oxygenated blood, resulting in **erythema**.
In **congestion**, diminished outflow leads to a capillary bed swollen with deoxygenated venous blood and resulting in **cyanosis**.



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Congestion

In chronic passive congestion, there will be:

1- **Stasis** of poorly oxygenated blood

2- Chronic **hypoxia** due to impaired circulation

3- **Degeneration & Death** of the parenchymal cells in that tissue

4- Persistent congestion of the capillaries will cause their rupture, resulting in **foci of hemorrhage**

5- Red cells fragments and necrotic tissue will be phagocytosed resulting in **aggregates of hemosiderin macrophages**

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Hemorrhage

- **Hemorrhage** simply means **bleeding**
- **Bleeding** may occur due to **clotting disorders**, or from **trauma**
- **Capillary bleeding** can occur because of **congestion**, **trauma**, or **inflammation**
- **Bleeding** may be **external** or **internal** (within the tissues)
- Collection of blood within a tissue is called **hematoma**. **Large hematomas can be fatal**

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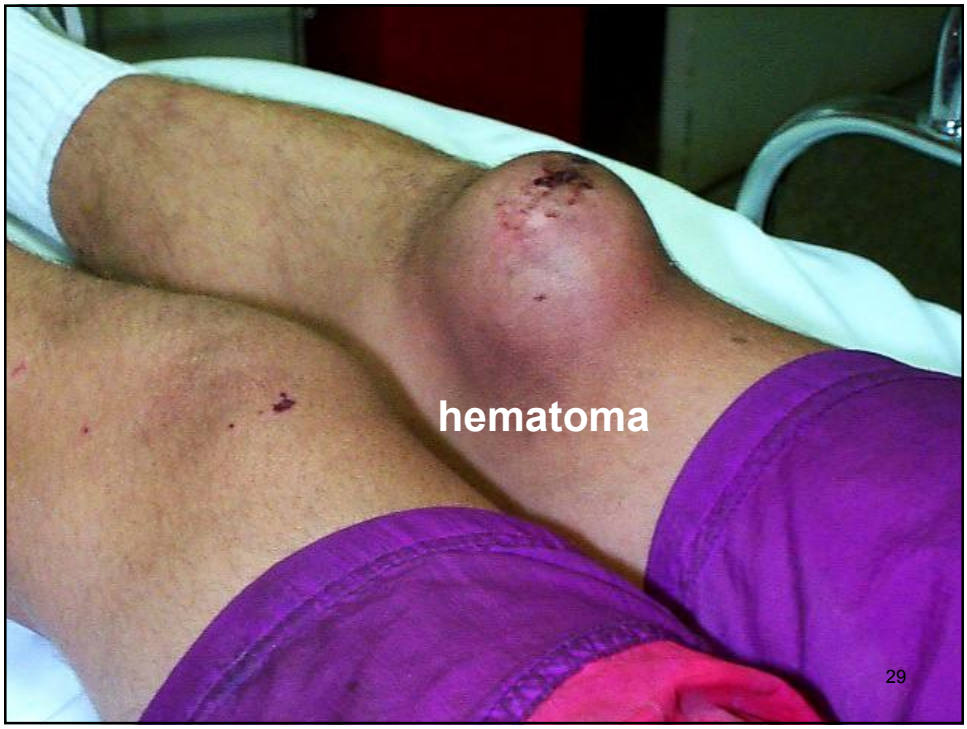
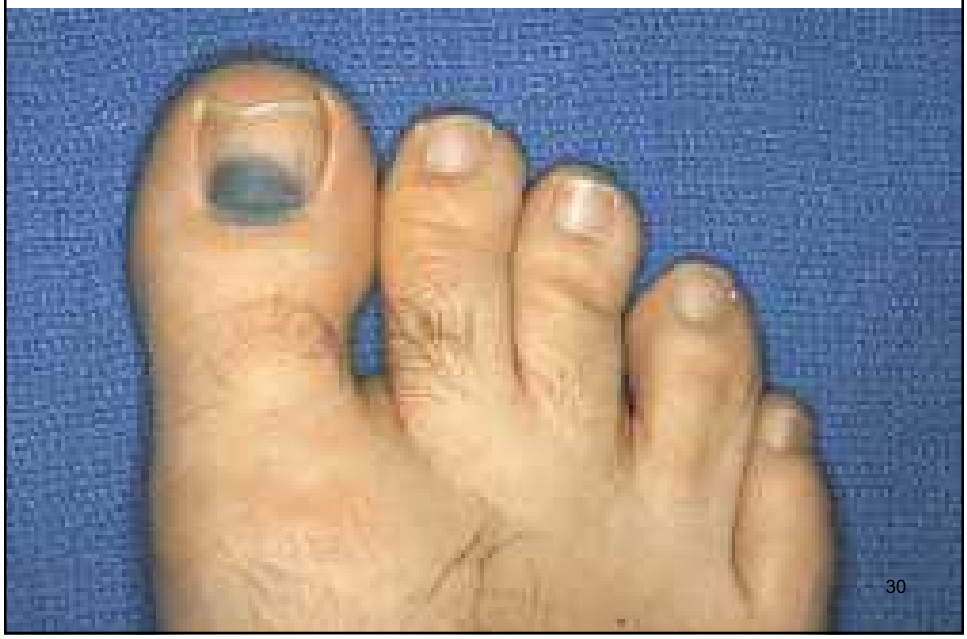


Nail bed - Hematoma



Hemorrhage

- Significance of bleeding **depends on:** the **amount** and the **place** where bleeding occurs.
- Small amounts of bleeding in the cranial cavity may be fatal, whereas, 1.5 liters of blood in the stomach may pass unnoticed by the patient.
- **Rapid bleeding** of up to **20%** of total body blood may be compensated for by the body and does not cause serious clinical manifestations
- **Slow bleeding** may result in **iron deficiency anemia**, particularly in elderly people

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Hemorrhage

- Small hemorrhages of **1-2 mm** into the skin or mucous membranes are called **petechiae**
- **Petechiae are caused because of:**

1- increased intravascular pressure

2- low platelet count

3- defective platelet function

4- clotting factor deficiency

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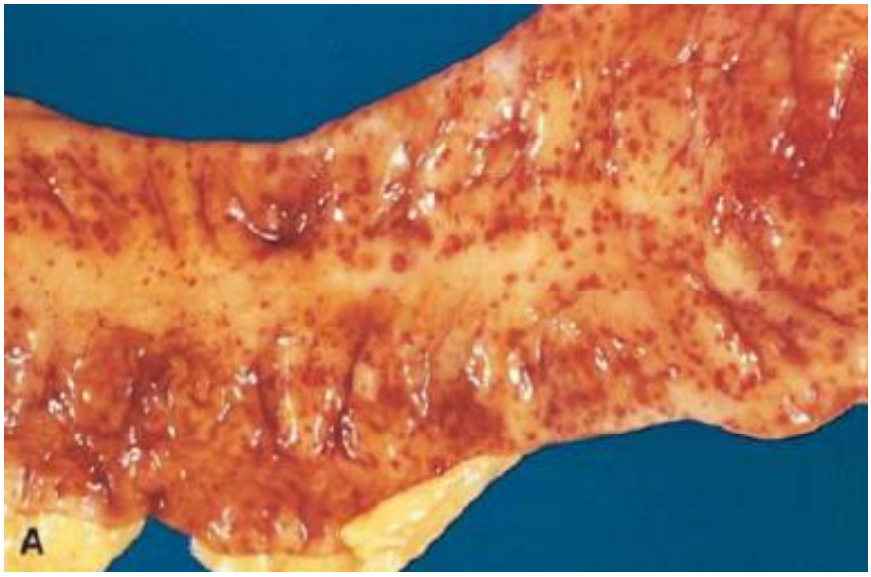


Petechial hemorrhages of the colonic mucosa, as a consequence of **thrombocytopenia**. 33

Hemorrhage

Purpuras: larger hemorrhages: **3-5 mm**

Causes:

1- increased intravascular pressure

2- **low platelet count**

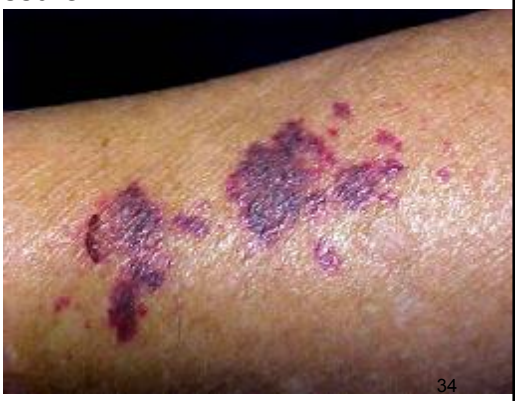
3- defective platelet function

4- **clotting factor deficiency**

5. vasculitis

6. increased vascular fragility

7. trauma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Hemorrhage

- **Ecchymosis**: are subcutaneous hematoma or **bruise**
  - They are **1-2 cm** in area
  - The **erythrocytes** in these hemorrhages are **phagocytosed** and degraded.
  - Their **hemoglobin (red-blue in color)** will be converted to **bilirubin**, which is **blue green** in color
  - Eventually, bilirubin will be converted to **hemosiderin**, a **golden-brown** colored material

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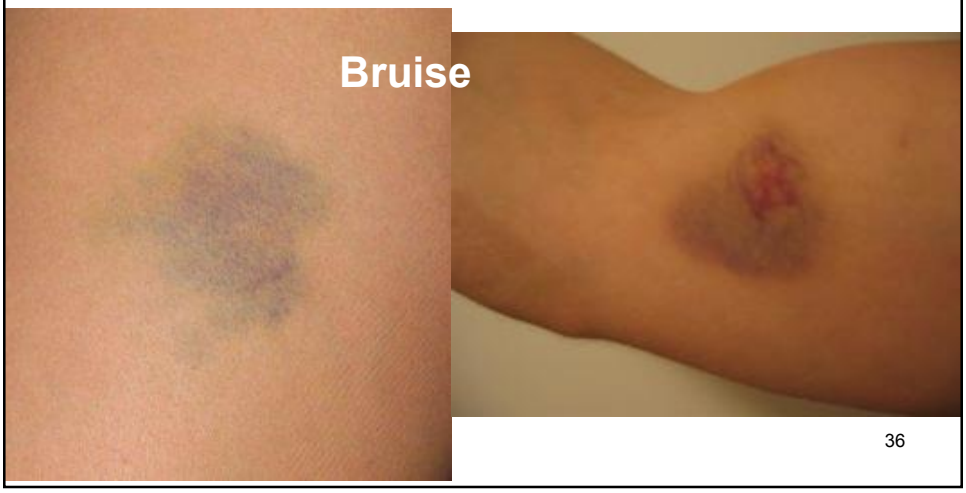
A **bruise or Ecchymosis** is a kind of injury, usually caused by blunt impact, in which the capillaries are damaged, allowing blood to seep into the surrounding tissue.



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Hemorrhage

Larger accumulations of blood:

1- hemothorax: blood in the pleural cavity

2- hemopericardium: blood in the pericardial cavity

3- hemoarthrosis: blood in the joint

4- hemoperitoneum: blood in the peritoneal cavity

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Infarction

- **Infarction** is an areas of **ischemic necrosis** that is caused by occlusion of either the **arterial** supply or the **venous** drainage in a particular tissue.
- **Examples:**
  - Myocardial infarction
  - Cerebral infarction
  - Pulmonary infarction
  - Bowel infarction
  - Extremities necrosis (gangrene)

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What vascular lesions lead to infarction?

- **Thrombosis**
- **Embolism**

99 %

- External compression
- Twisting of pedicle
- Arterial spasm
- Hemorrhage from a trauma

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Uncommon causes of infarction

- **Vasospasm of vessels**: coronaries in Prinzmetal angina
- **Compression** from outside by tumors or edema
- **Twisting** of the vessels as in torsion of testis or intestinal intussusception or volvulus
- **Entrapment** of vessels as in strangulated hernia
- **Traumatic** rupture of the blood supply

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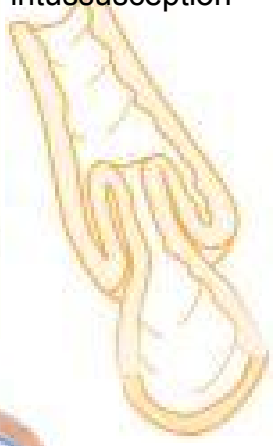
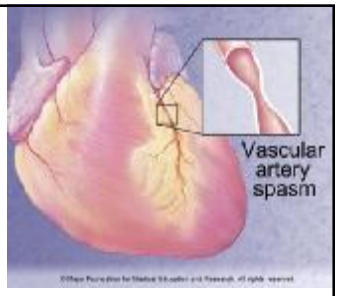
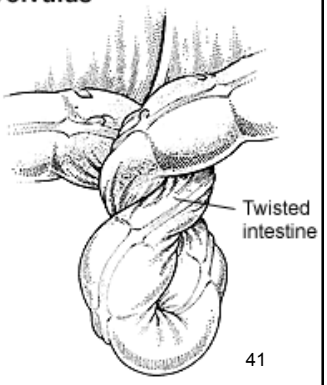
torsion of testis

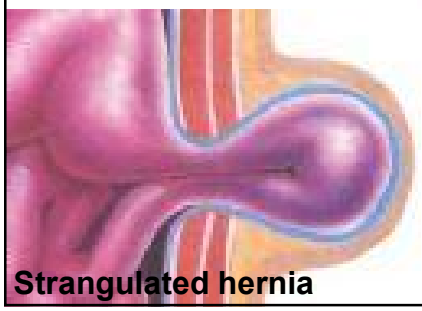
Intestinal intussusception





Volvulus





Strangulated hernia

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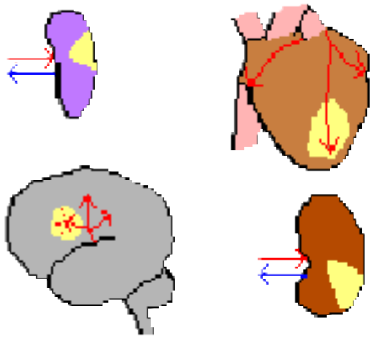
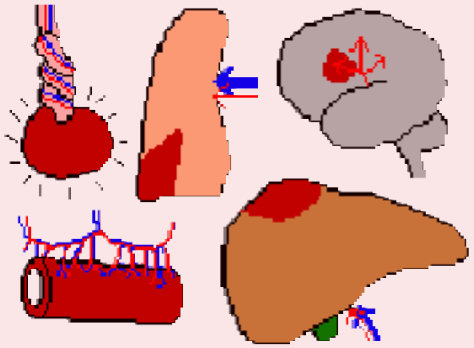
White Infarcts



Arteral Insufficiency
AND
Not Reperfused
AND
Single Blood Supply

Red Infarcts



Venous Insufficiency
OR
Reperfused
OR
Dual Blood Supply

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Types of Infarcts

- **White infarcts (anemic):** occurs in **arterial occlusions** or in **solid organs** (such as heart, spleen, and kidney)
- **Shape of infarcts:**
  - Infarcts are generally **wedge shaped**. The apex of the wedge is at the site of the occluded vessel, and the base points towards the periphery of the organ
  - If the base of the infarcts is a serous surface, there will be **fibrinous exudate** on that surface

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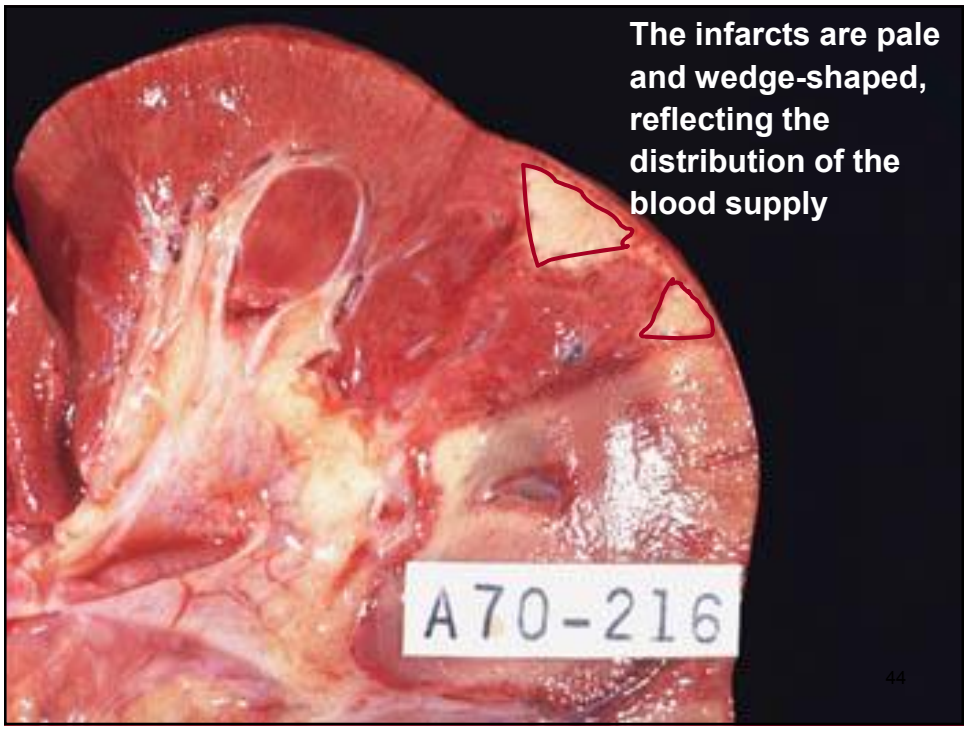

The infarcts are pale and wedge-shaped, reflecting the distribution of the blood supply

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Types of Infarcts

Red infarcts: are hemorrhagic infarcts and occur:

1) In **loose** tissues like lung that permits collection of blood
2) In tissues with **dual blood supply**: like in the lungs and intestine
3) In **venous occlusion** (e.g. ovarian torsions)
4) In tissues that are already congested from impaired **venous** flow (e.g. liver **congestion**)
5) In **reperfusion** of tissues after arterial occlusion that has caused necrosis

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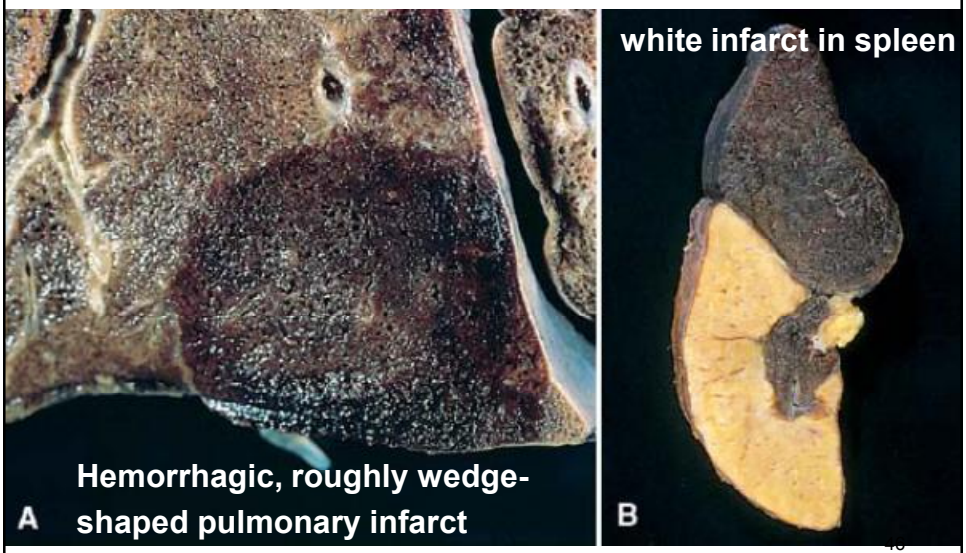
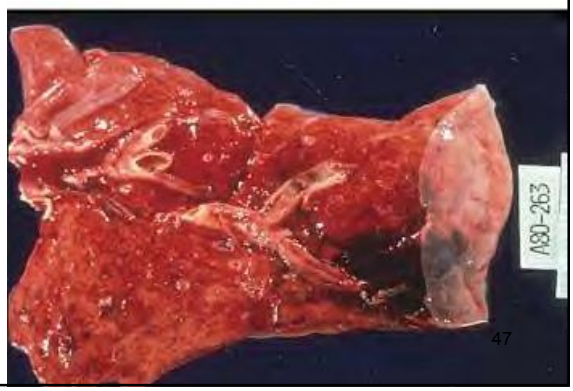
Examples of Infarction



PULMONARY INFARCT

- EMBOLIZATION TO SMALL DISTAL VESSELS IN LUNG MAY CAUSE **ISCHEMIC NECROSIS** OF TISSUE OR **INFARCT**



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Factors that affect development of infarct:

1. **Nature of the vascular supply**:

That's why organs with dual blood supply do not develop infarctions if there is obstruction to small blood vessels

- The lung has pulmonary and bronchial blood supply
- Upper extremities with radial and ulnar blood supply
- Whereas organs such as spleen, kidney, and the eye has end-arterial blood supply

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Factors that affect development of infarct:

2. **Rate of development of occlusion:**
   - Slowly developing occlusion may give time for alternative pathway
3. **Susceptibility of involved tissue to hypoxia:**
   - **Neurons** undergo irreversible damage if they are deprived of their blood supply for only 3-4 minutes
   - **Myocardial cells** die after 20-30 minutes
4. **Oxygen content of the blood:**
   - **Cyanotic** patients or **anemics** are more likely to develop infarction as compared to normal people

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Hemostasis & Thrombosis

- **Normal Hemostasis:** the process by which the blood is maintained in a clot-free fluid state and produces a local hemostatic plug at sites of vascular injury
- **Thrombosis:** inappropriate activation of the hemostatic process in uninjured vasculature or formation of **thrombus** in the setting of relatively minimal vascular injury

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Hemostasis:

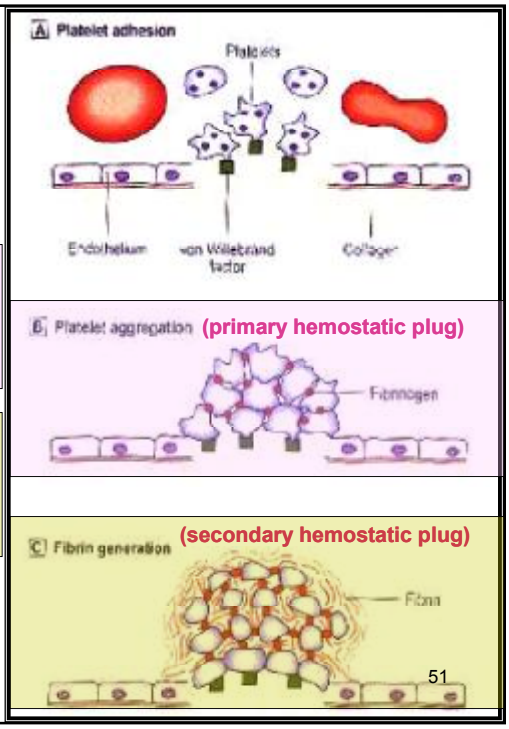
- Vasoconstriction
- Platelet activation

Primary hemostasis

- Platelet aggregation
- Coagulation cascade

Secondary hemostasis

- Stable clot formation
- Clot dissolution



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Sequence of hemostasis:

I- Vasoconstriction

- Immediately after injury there is an initial ***vasoconstriction***.
- This is stimulated by the release of ***endothelin*** from the endothelial cells.
- The *endothelin* is an important vasoconstrictor

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Sequence of hemostasis:

II- Primary hemostasis

- ***Activation & adherence of platelets:*** Platelets adhere to exposed extracellular matrix (ECM) via von Willebrand factor (**vWF**) and are activated.
- Activated platelets undergo a shape change and granule release; released ADP and thromboxane A2 (TXA2) lead to further ***platelet aggregation***, to form **the primary hemostatic plug**.

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Sequence of hemostasis:

III- Secondary hemostasis

- Local activation of the coagulation cascade (involving **tissue factor** and platelet phospholipids) results in fibrin polymerization, reinforcing the platelets into a definitive **secondary hemostatic plug**.
- ***The tissue factor*** **(cellular lipoprotein)** ***has the following characteristics:***
  - **is a pro-coagulant factor**
  - **synthesized by endothelium**
  - **is released at the site of injury**

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Sequence of hemostasis:

IV- Antithrombotic counter regulation

- Anticoagulation mechanism is triggered after the formation of permanent clot by polymerization of fibrin and aggregation of platelets
- Counter-regulatory mechanisms, such as release of ***Tissue plasminogen activator*** (**t-PA,** a fibrinolytic product) and **thrombomodulin** (interfering with the coagulation cascade), are activated to prevent further expansion of the clot and limit the hemostatic process to the site of injury.

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Hemostasis & Thrombosis

Components:

- **Both hemostasis and thrombosis are dependent on:**
  1. **The vascular wall (Endothelium)**
  2. **Platelets**
  3. **The coagulation cascade**

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1. Endothelium

- **The endothelial cells normally posses:**

  antiplatelet, anticoagulation, and fibrinolytic properties

- **If the endothelial cells are injured or activated,**

  they develop pro-coagulant functions

- **These activators** increase procoagulant activity, and decrease anticoagulant activity

- **Examples of endothelial cells activators:**

  1- Cytokines: IL-1 and TNF

  2- Plasma mediators

  3- Infectious agents

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Endothelial cells synthesize:

- **Endothelin:** vasoconstrictor
- **Tissue factor**: activate the coagulation cascade, the extrinsic pathway
- **PGI_2** & **NO**: vasodilators and inhibit platelet aggregation
- **Adenosine diphosphatase:** degrades ADP and inhibits platelet aggregation
- **Heparin like molecules**: allow antithrombin to inactivate thrombin, factor Xa, and other caogulation factors
- **Thrombomodulin**: convert thrombin from procoagulant to anticoagulant
- **t-PA**: promotes fibrinolysis of the fibrin clot
- **vWF:** that helps bind platelets to collagen

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Antithrombotic properties of endothelium:

- **Antiplatelet effects**
- **Anticoagulant properties**
- **Fibrinolytic properties**

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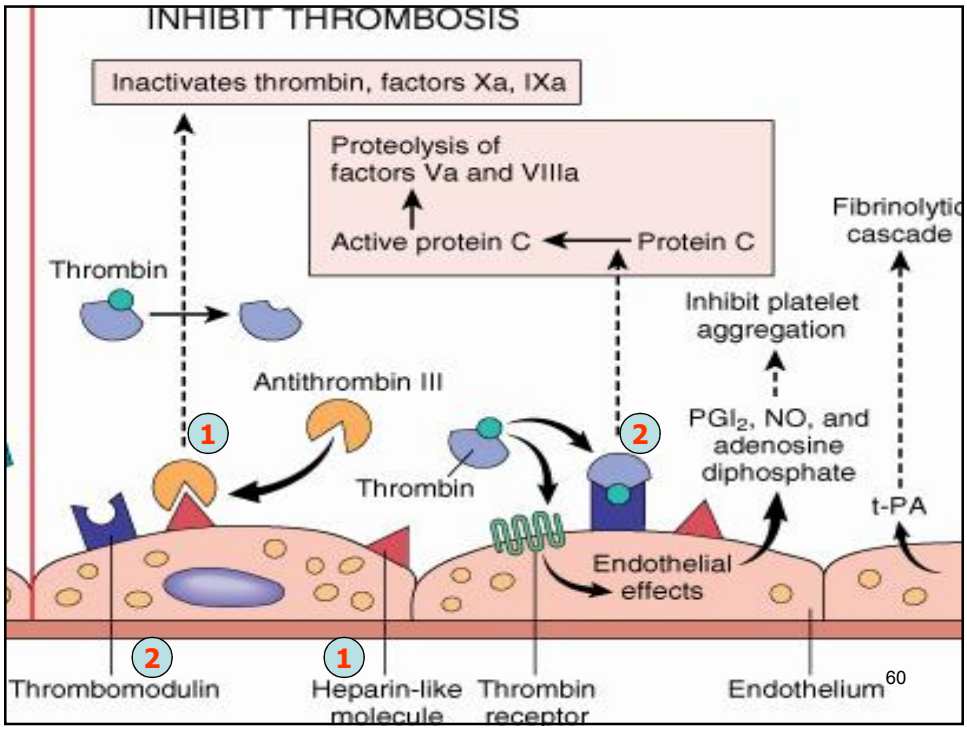

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Prothrombotic properties of endothelium

Intact endothelial cells serve primarily to inhibit platelet adherence & blood clotting. However, injury or activation of endothelial cells results in a procoagulant phenotype that contributes to localized clot formation:

- Platelets **adhere** to the exposed sub-endothelial collagen. This is facilitated **by vWF** secreted by endothelial cells
- Endothelial cells **secrete tissue factor** which activates the extrinsic clotting pathway
- Endothelium **secretes plasminogen activator inhibitors** which depress fibrinolysis

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2. Platelets

- At injury site, platelets come in contact with ECM and they undergo ***three general reactions***:

1- Adhesion and shape change

2- Secretion

3- Aggregation

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Platelets

Platelet adhesion:

- **Adhesion** of platelets **with collagen** in the ECM at the time of injury is facilitated **by vWF**.
- vWF act as a bridge between platelet surface receptors and exposed collagen
- Genetic deficiencies of vWF (von Willebrand disease) or its receptors result in serious bleeding disorders.

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Platelets

Platelet aggregation:

- The vasoconstrictor thromboxane A2 (TXA2, secreted by platelets) is a potent stimulus for platelet aggregation. This is the primary hemostatic plug and is reversible
- **Thrombin** formed in the coagulation cascade, binds to platelet surface and with **ADP** and **TXA2** causes further platelet aggregation, followed by platelet contraction and becoming irreversible (secondary hemostatic plug)
- Thrombin convert **fribrinogen** to **fibrin** that adds to cementing of the platelet plug

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Platelets

Platelet aggregation:

- **The clinical use of aspirin (a cyclooxygenase inhibitor) in patients at risk for coronary thrombosis is related to its ability to inhibit the synthesis of TXA2.**

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3. Coagulation Cascade

- **It's composed of two pathways:**
  1. The **intrinsic pathway** initiated by the activation of Hageman factor
  2. The **extrinsic pathway** which is activated by the tissue factor
- It's a series of reactions in which inactive proenzymes are converted into active enzymes
- This results in the formation of **thrombin**, that converts the soluble fibrinogen into insoluble **fibrin**

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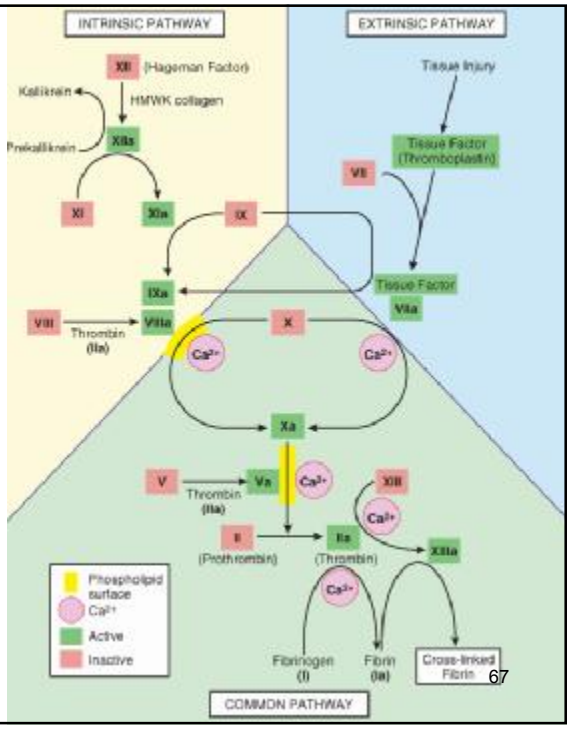
Coagulation cascade

Note the common link between the intrinsic and extrinsic pathways at the level of factor IX activation

Factors in red boxes represent inactive molecules

Activated factors are indicated with **lower-case *a*** and green box.

HMWK: high-molecular-weight kininogen.



Coagulation Cascade:

Intrinsic Pathway (12, 11, 9, 8)

Extrinsic Pathway Tissue factor, (7)

(Factor 10)

Common Pathway (5,2)

Prothrombin→ Thrombin

Fibrinogen → Fibrin

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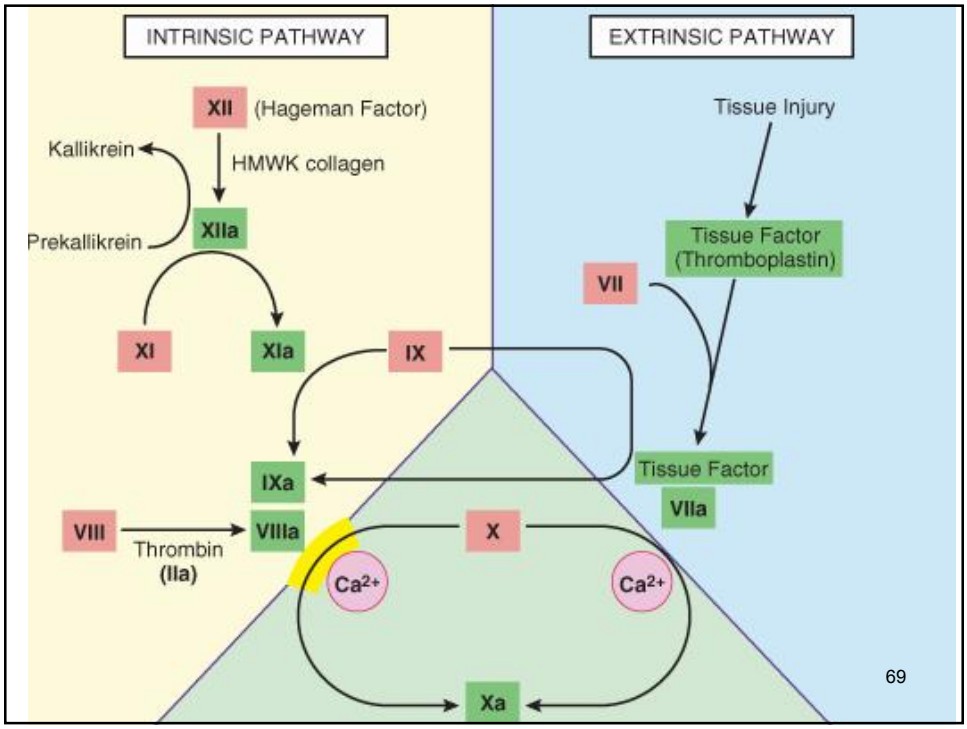
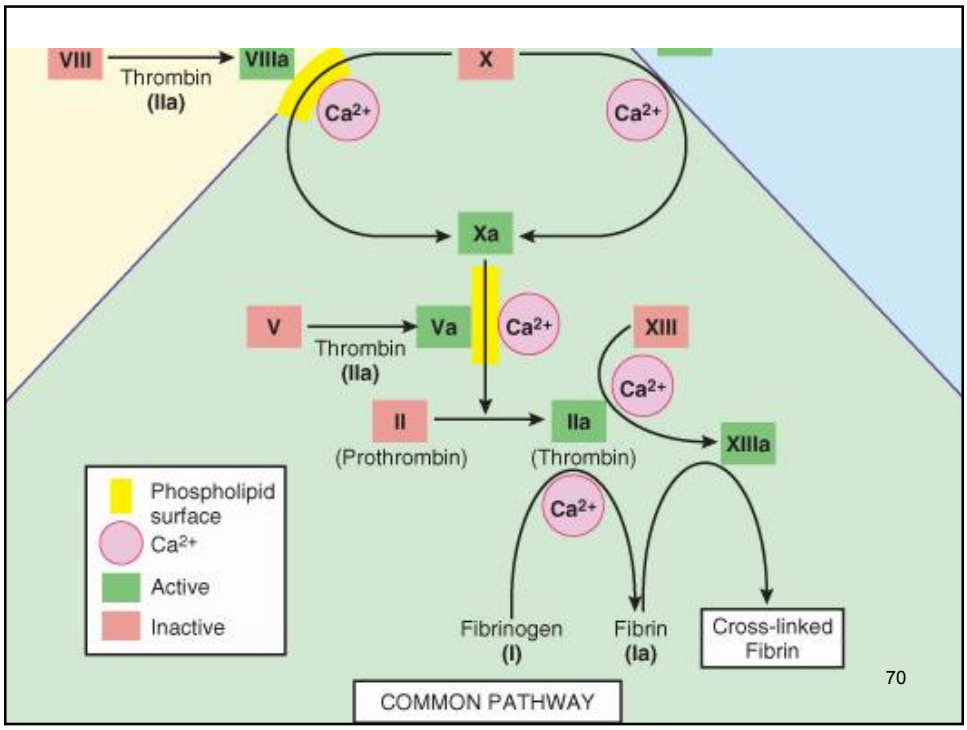
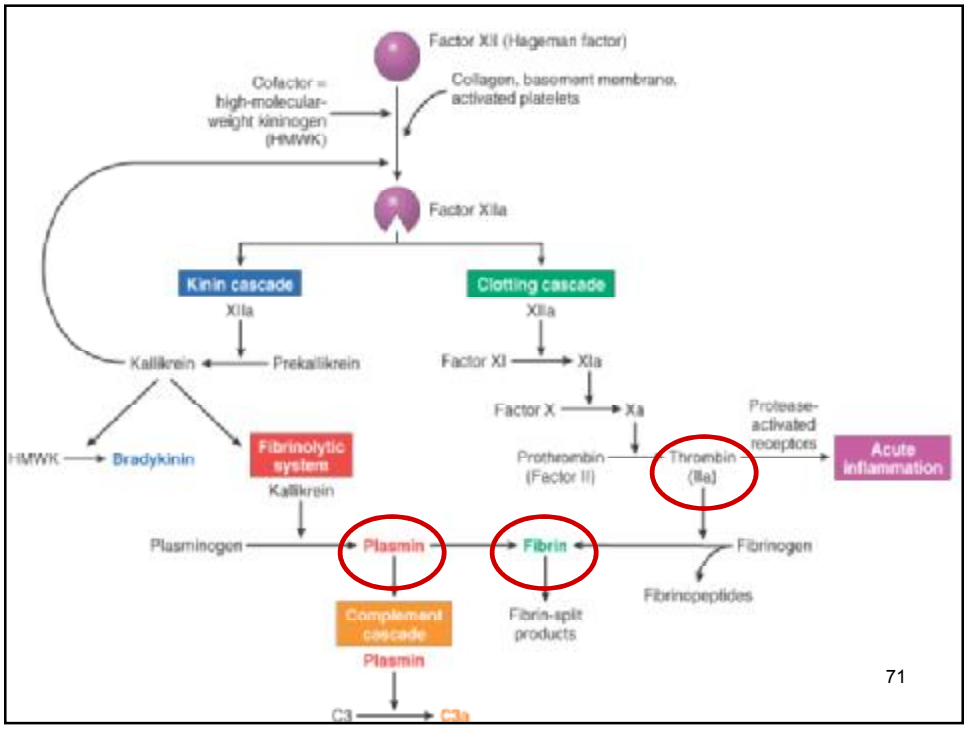

INTRINSIC PATHWAY
EXTRINSIC PATHWAY
XII (Hageman Factor)
Kallikrein
HMWK collagen
Prekallikrein
XIIa
XI
XIa
IX
Tissue Injury
Tissue Factor (Thromboplastin)
VII
IXa
Tissue Factor
VIIa
VIII
Thrombin (IIa)
VIIIa
X
Ca2+
Ca2+
Xa
69


VIII
Thrombin (IIa)
VIIIa
X
Ca2+
Ca2+
Xa
V
Thrombin (IIa)
Va
Ca2+
XIII
Ca2+
II
(Prothrombin)
IIa
(Thrombin)
XIIIa
Ca2+
Phospholipid surface
Ca2+
Active
Inactive
Fibrinogen (I)
Fibrin (Ia)
Cross-linked Fibrin
COMMON PATHWAY
70



Coagulation Cascade

- Clotting is regulated in a way to be confined to the site of injury by **two natural anticoagulants**:

1. **Antithrombins: (e.g., antithrombin III)**

- It inhibits the activity of thrombin, factor IXa, Xa, XIa, & XIIa
- Antithrombin is activated by binding to heparin like molecules on endothelial cells

2. **Protein C and S:**

- They are two **vitamin K dependent** proteins
- They inactivate cofactors Va and VIIIa

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Fibrinolytic Cascade

- Besides inducing coagulation, activation of the clotting cascade also sets into motion a *fibrinolytic cascade* that will limit the size of the final clot by activation of ***plasmin***.
- **Plasmin** is obtained from the precursor plasminogen either by XIIa or by plasminogen activators (mainly t-PA)
- **Plasmin** breaks down fibrin producing fibrin split products (also called fibrin degradation products)
- Fibrinolysis is blocked by *Plasminogen activator inhibitors*

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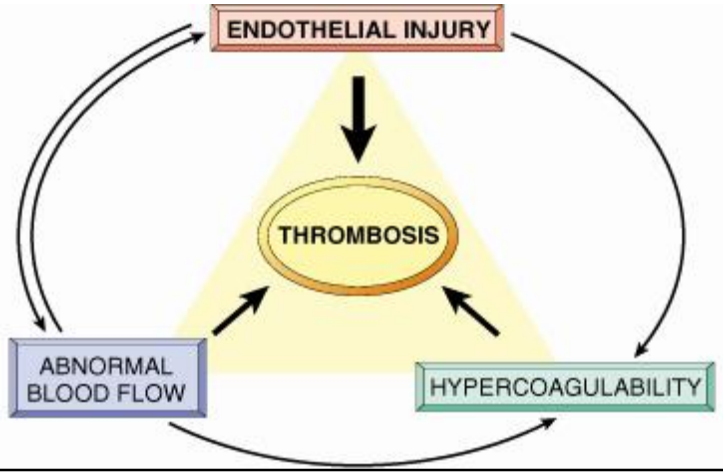
Thrombosis

Virchow triad in thrombosis are:

1. **Endothelial injury**
2. **Blood hypercoagulability**
3. **Stasis or turbulence of blood flow**



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1. The endothelial cell injury:

- Loss of endothelium leads to exposure of ECM, adherence of platelets, release of tissue factor, local depletion of PGI2 and t-PA
- Particularly important in thrombus formation in the heart and arterial circulation
- Dysfunctional endothelium may elaborate greater amounts of procoagulant factors (e.g., adhesion molecules to bind platelets, tissue factor) and smaller amounts of anticoagulant effectors (e.g., thrombomodulin, PGI2, t-PA).

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The endothelial cell injury

Causes of endothelial cell injury:

- Physical disruption
- Hypertension
- Turbulent flow over scarred valves
- Bacterial endotoxins
- Radiation
- Hypercholesterolemia
- Toxic substances (e.g., cigarette smoke)

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2. Alteration in normal blood flow:

- Flow of platelets in the blood is laminar
- **Turbulence or stasis will result in:**
  1) bring platelets into contact with the endothelium
  2) prevent dilution of activated clotting factors by fresh-flowing blood
  3) promote endothelial cell activation, predisposing to local thrombosis and leukocyte adhesion
  4) delay the inflow of clotting factor inhibitors and permit the build-up of thrombi

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3. Hypercoagulability:

- **Conditions associated with an increased risk of thrombosis**

Primary (Genetic) causes:

1- Factor V mutations

2- Prothrombin mutations

3- Antithrombin III deficiency

4- Protein C and S deficiency

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Hypercoagulability:

- **Secondary (Acquired) causes:**

Examples:

1. Prolonged bed rest or immobilization
2. Myocardial infarction
3. Tissue damage (surgery, fracture, burns)
4. Cancer
5. Prosthetic cardiac valves
6. Disseminated intravascular coagulation
7. Lupus anticoagulant

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Thrombosis: MORPHOLOGY

- Thrombi may develop anywhere in the cardiovascular system
- Thrombi are of variable size and shape
- An area of attachment to the underlying vessel or heart wall, frequently firmest at the point of origin, is characteristic of all thrombi.
- **Thrombi are significant because:**

1) they cause **obstruction** of arteries and veins

2) they are possible sources of **emboli**

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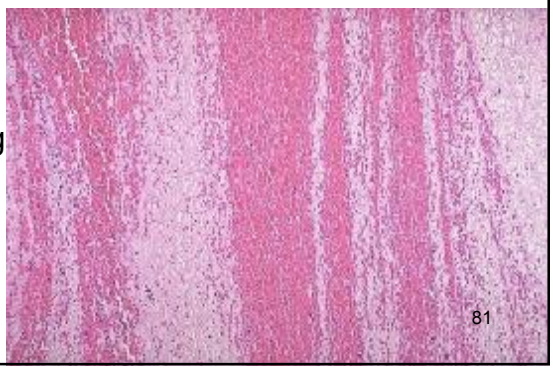
Thrombosis in heart chambers & aorta

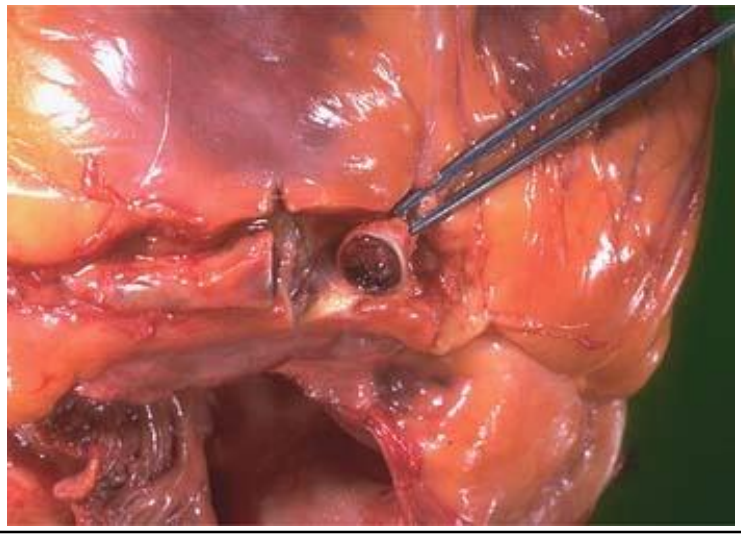
- **Mural thrombi** are those thrombi that form on the walls of the **heart chambers and aorta**
- **Causes:** arrhythmias, dilated cardiomyopathy, MI, myocarditis, catheter trauma

Lines of Zahn

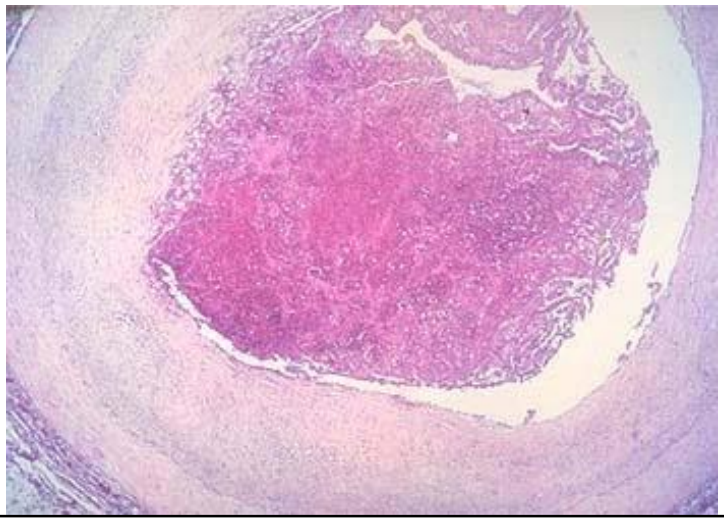
produced due to alternating pale layers of platelets and fibrin with dark layers of RBC in thrombi formed in the heart or aorta



Coronary artery, right, with thrombus filling and completely occluding the lumen. Thrombi in coronary arteries are **almost always** due to endothelial damage resulting **from atherosclerosis**.



Cross section of a coronary artery. The intima, to which a thrombus is attached, is markedly thickened by atherosclerosis. The thrombus nearly fills the lumen, but in one area, it has retracted from the vessel wall.



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Venous thrombosis (phlebothrombosis)

- Characteristically occur in sites of stasis
- may not be well attached and are prone to emboli
- They contain more RBCs, therefore known as **red,** or **stasis, thrombi**
- 90% of cases involve the veins of lower extremities

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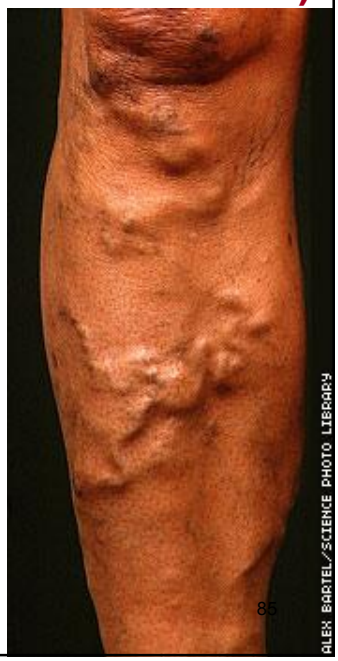
Venous thrombosis (phlebothrombosis)

- Superficial venous thrombi usually occur in the saphenous system, particularly in varicosities
- **Superficial thrombi** may cause swelling and pain but seldom embolize



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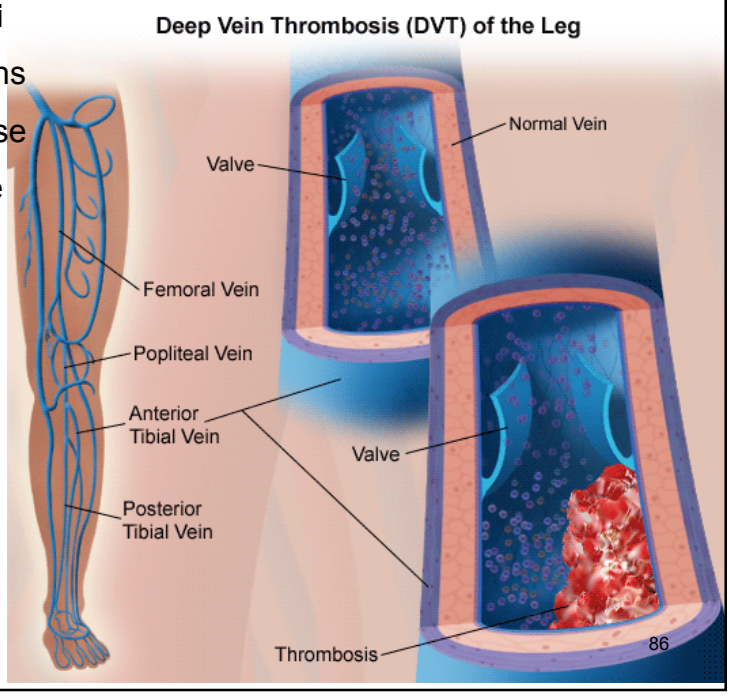
- **Deep thrombi** in the large veins particularly those above the knee joint in the popliteal, femoral, & iliac veins are more serious as they may embolize **(Where ?)**



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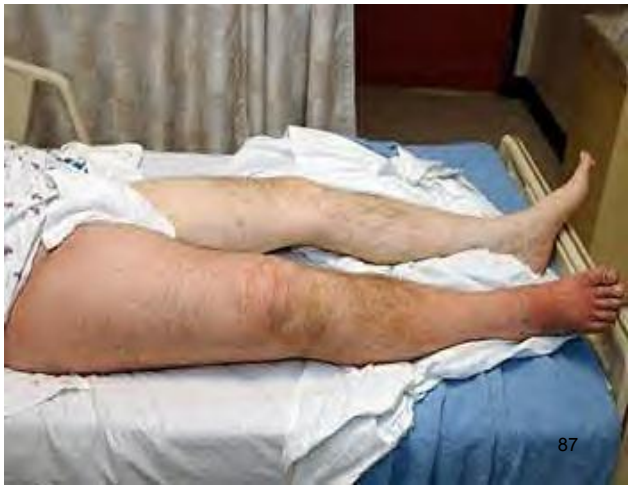
Deep Vein Thrombosis (DVT)

deep venous thromboses are asymptomatic in 50% of cases. Advanced age, bed rest, and immobilization increase the risk of deep vein thrombosis



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Fate of Thrombus

1. **Propagation:** thrombi may accumulate more fibrin & platelets causing obstruction
2. **Embolization:** thrombi may detached and be transported to other sites in the vasculature
3. **Dissolution:** thrombi may be removed by fibrinolytic activity
4. **Organization and Recanalization:** Thrombi may induce inflammation and fibrosis ***(organization)*** and may become ***recanalized*** (re-establish vascular flow), or they may be incorporated into a thickened vascular wall. (in old thrombi)

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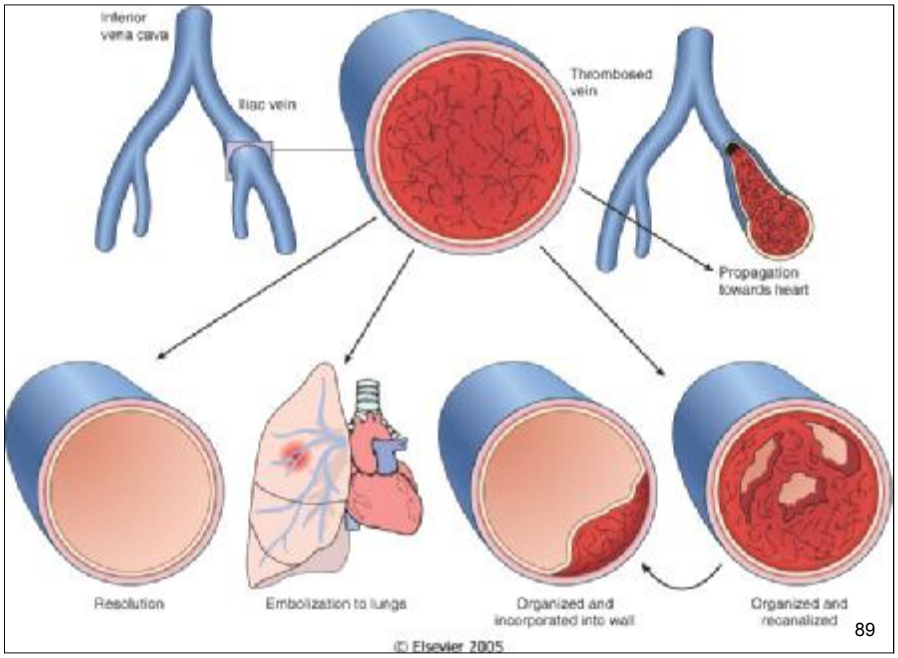

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Vein with organizing and recanalizing thrombus
Filling this vessel is a red thrombus attached to the vessel wall. In one area, it has retracted, forming a crescent-shaped lumen

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Embolism:

- Abnormal solid mass carried in blood.
- Types.
  - **Thromboembolism** - atherosclerosis
  - **Fat** - Fractures
  - **Gas** – 'Caisson disease'
  - **Liquid** – Amniotic fluid
- Outcome of Embolism
  - Collateral circulation
  - Infarction
  - Hemorrhage

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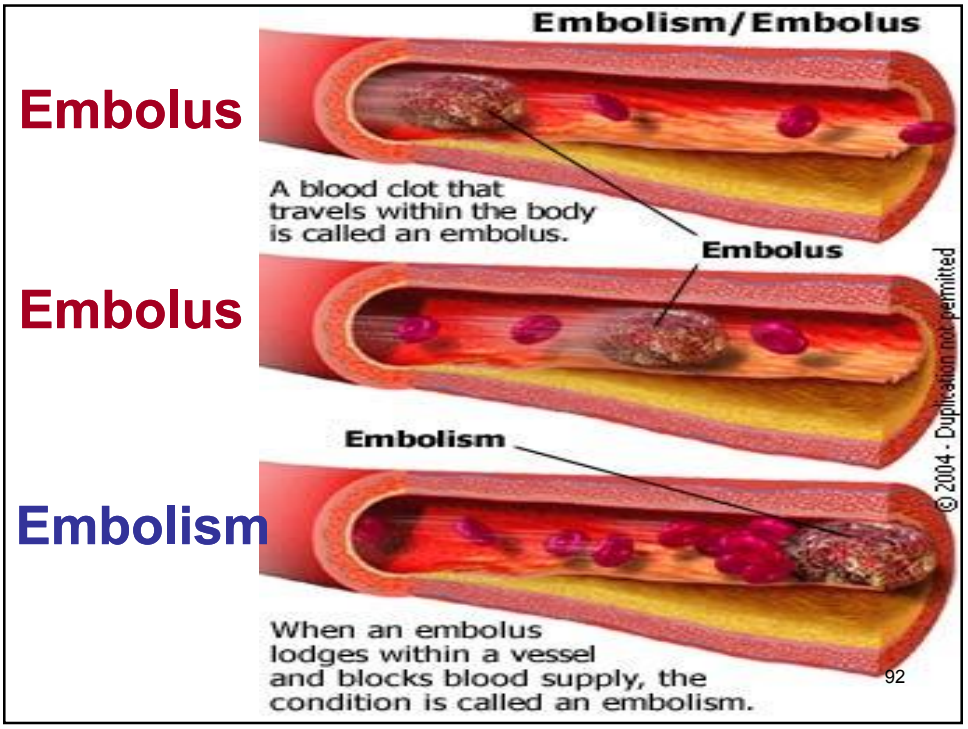

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Embolism

- An **embolus** is a detached intravascular **solid**, **liquid**, or **gaseous mass** that is carried by the blood to a site distant from its point of origin
- **99%** of all emboli represent part of thrombus, hence the commonly used term **thromboembolism**
- **Rare forms of emboli include:**

  droplets of fat, bubbles of air or nitrogen, atherosclerotic *(cholesterol emboli),* tumor fragments, bits of bone marrow, or foreign bodies such as bullets.

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Pulmonary Thromboembolism

- It is common in hospitalized patients
- Originates mainly in deep veins of the lower extremities
- Emboli travel to the right side of the heart to the pulmonary arteries
- May be so large to block the main pulmonary artery at the site of bifurcation, called **saddle embolus**
- May be small to pass into smaller branches

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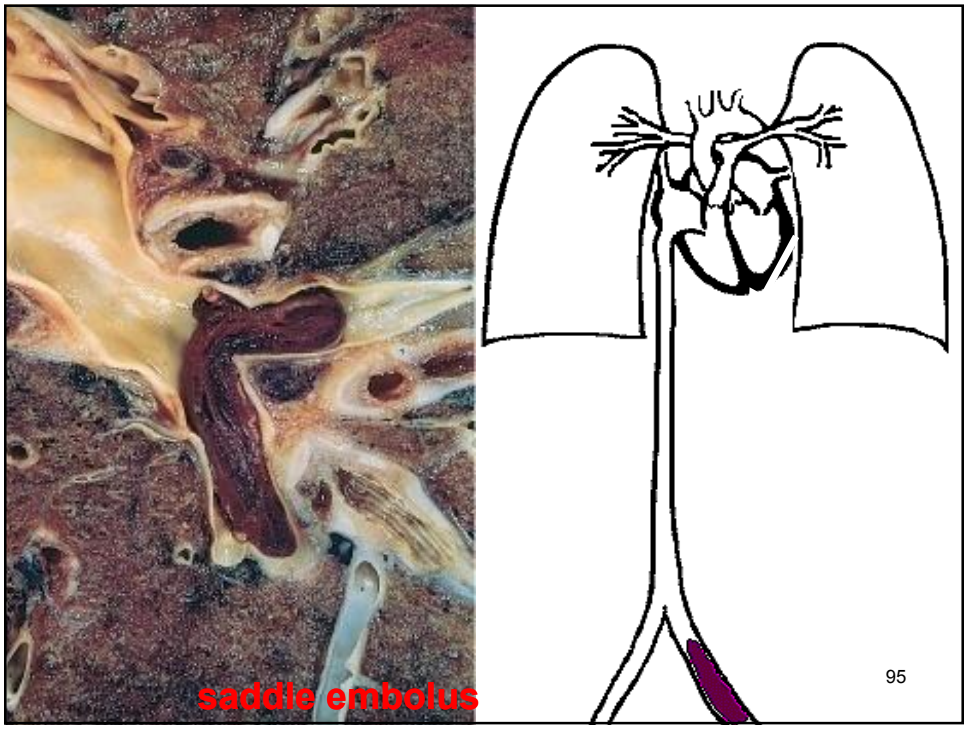

Fate of pulmonary embolism

- Sudden death, right ventricular failure, or cardiovascular collapse occur when 60% or more of the pulmonary circulation is obstructed with emboli.
- 60-80% are **clinically silent** because they are small, undergo dissolution or recanalization
- Embolic obstruction of medium-sized arteries may result in **pulmonary hemorrhage**
- Multiple emboli over time may cause **pulmonary hypertension** with right ventricular failure

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Systemic Thromboembolism

- Refers to emboli traveling within the **arterial** circulation
- 80% arise from intra-cardiac mural thrombi associated with **left ventricular** wall infarcts (2/3),with dilated **left atria** (1/3)
- **The rest originates from**:
  - **Atherosclerosis** in aorta or from aortic aneurysms
  - **Paradoxical embolism:** rarely, emboli may travel from venous to arterial circulation via a communication between arterial & venous circulation
- **Major sites for lodging of systemic emboli:**

the lower extremities (75%) and the brain (10%)

- arterial emboli cause **infarction** of tissues in the distribution of the obstructed vessel.

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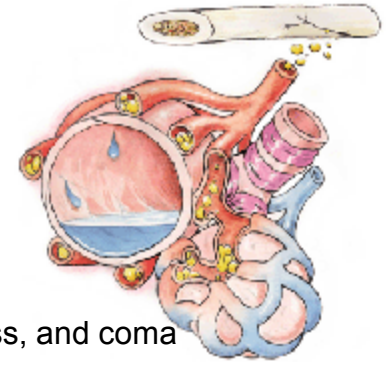
Fat Embolism

- **Etiology:** mainly after fractures of long bones or, rarely, in the setting of soft tissue trauma and burns



Fat embolism syndrome:

- Fatal in about 10% of cases
- Respiratory: tachypnea, dyspnea
- Neurological: irritability, restlessness, and coma
- Thrombocytopenia with characteristic petechiae
- It generally develops 1 to 3 days after injury
- The pathogenesis involves both mechanical obstruction and toxic injury to endothelium by FFA

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Fat Embolism

The fat embolus enters the circulation from marrow after rupture of bone vascular sinusoids, or from adipose tissue through rupture of tissue venules

Bone marrow embolus in the pulmonary circulation, the cleared vacuoles represent marrow fat

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Air Embolism

- Air may enter the circulation during surgical obstetric procedures or as a consequence of chest wall injury
- Generally, > 100 mL of air is required to produce a clinical effect
- may cause focal ischemia in the brain and heart
- may cause edema, hemorrhages, and focal atelectasis or emphysema, leading to respiratory distress in the lungs

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Amniotic Fluid Embolism

- The underlying cause is the leakage of amniotic fluid (and its contents) into the maternal circulation via a tear in the placental membranes and rupture of uterine veins.
- The presence of the followings in the pulmonary circulation will confirm the diagnosis:
  - Squamous cells from fetal skin
  - Lanugo hair
  - mucin derived from fetal respiratory or GI tracts

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Shock (cardiovascular collapse)

- Systemic hypoperfusion due to a reduction either in cardiac output or in the effective circulating blood volume
- **Types of shock:**
  1. **Cardiogenic shock**
     - Pump failure
  2. **Hemorrhagic (hypovolemic) shock**
     - Decrease in blood volume
  3. **Septic shock**
     - Failure of microcirculation to retain pressure leading to wide spread peripheral vasodilatation

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I- Cardiogenic shock

- Failure of myocardial pump owing to intrinsic myocardial damage, extrinsic pressure, or obstruction to outflow

- **Causes:**
  1. myocardial infarction
  2. cardiac tamponade
  3. outflow obstruction in pulmonary embolism
  4. ventricular arrhythmia
- **Signs and symptoms:**
  - Tachycardia
  - Hypotension
  - Tachypnea
  - Restlessness, agitation
  - Pallor & sweating

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II. Hypovolemic shock

- Results from loss of blood or plasma volume
- **Causes:**

1. Hemorrhage
2. Fluid loss from severe vomiting, diarrhea, burns, or trauma

- Signs and symptoms of hypovolemic shock are the same as in cardiogenic shock

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III. Septic Shock

- Results from spread of an initially localized infection (e.g., abscess, peritonitis, pneumonia) into the bloodstream.
- Occurs when an overwhelming infection leads to low blood pressure, and vital organs may not function properly
- Has 25% to 50% mortality rate
- One of the most common causes of death in intensive care units
- **Caused by systemic microbial infection:**
  - Most commonly (~ 70%), **gram-negative** infections *(endotoxic shock)*
  - can also occur with gram-positive and fungal infections

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Pathogenesis of Septic Shock

- Endotoxins are bacterial wall lipopolysaccharides (LPSs)
- LPS activate mononuclear cell with production of chemical mediators
- The collective effect of these mediators result in:
  - Fever, acute-phase reaction, neutrophilia
  - Vasodilation: hypotension
  - Widespread endothelial cell injury
  - Activation of the coagulation system
  - Multiorgan system failure

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Shock (less common types)

Neurogenic shock:

- hemodynamic shock due to **loss of vascular tone** and peripheral pooling of blood resulting in vasodialtion
- **Causes**: spinal cord injury or trauma

Anaphylactic shock:

- initiated by a generalized immunoglobulin E-mediated hypersensitivity response
- associated with **systemic vasodilatation** and increased vascular permeability
- causes a sudden increase in the capacity of the vascular bed, which cannot be filled adequately by the normal circulating blood volume. Thus, tissue hypoperfusion and cellular anoxia result.

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Stages of Shock

- **Initial nonprogressive stage:** the causative factors of shock are contained and perfusion of vital organs is maintained (adequate compensatory mechanism)
- **Progressive stage:** tissue **hypoperfusion** continues resulting in tissue **hypoxia**, and metabolic disturbances (e.g., anaerobic glycolysis produced lactic acidosis). Compensatory mechanism is no longer adequate
- **Irreversible stage:** the patient has multiple organ failure, and death becomes inevitable

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