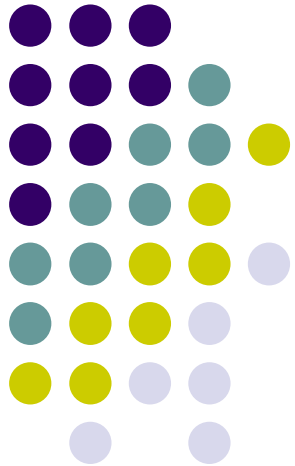
Hemodynamic Disorders, Thrombosis & Shock

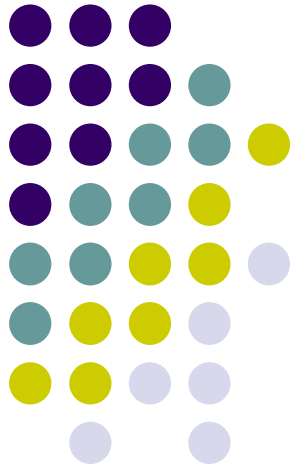
- Hemorrhage
- Hemostasis & Thrombosis
- Embolism
- Infarction
- Hyperemia and Congestion
- Shock



Hemorrhage

Extravasation of blood

due to rupture of blood vessels



Hemorrhage

Causes:

- Rupture of a large vessel:
  - Trauma
  - Atherosclerosis
  - Inflammatory
  - Neoplastic Erosion
- Rupture of small vessels:
  - hemorrhagic diathesis

Forms:

May be:

- external
- into a body cavity
- into a tissue

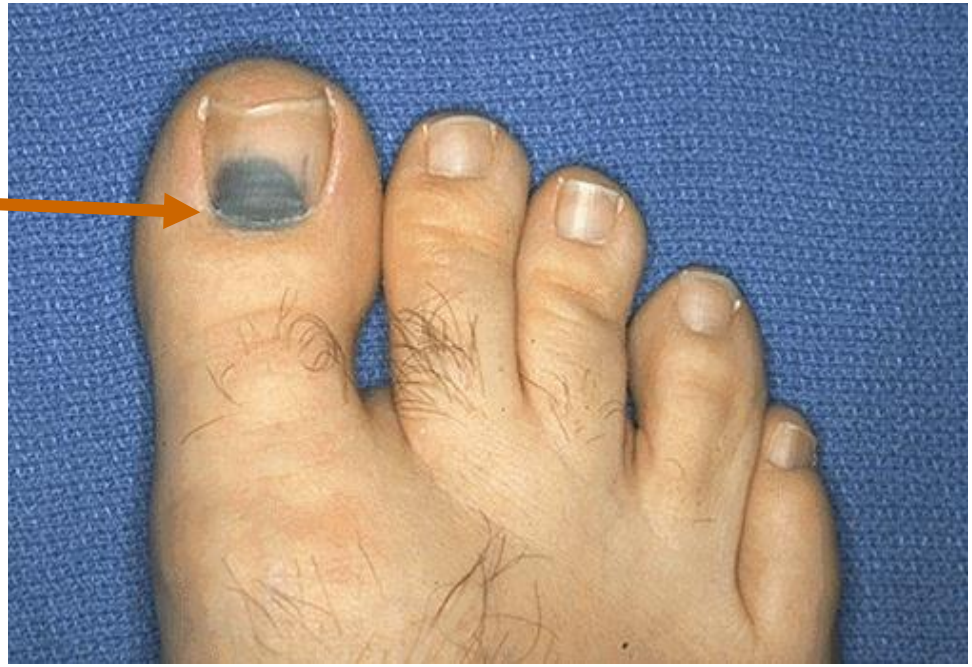
Hemorrhage

1) Hematoma:

accumulation of blood enclosed or confined within tissue

e.g.

- **Bruise** (insignificant)



- **retroperitoneal hematoma**

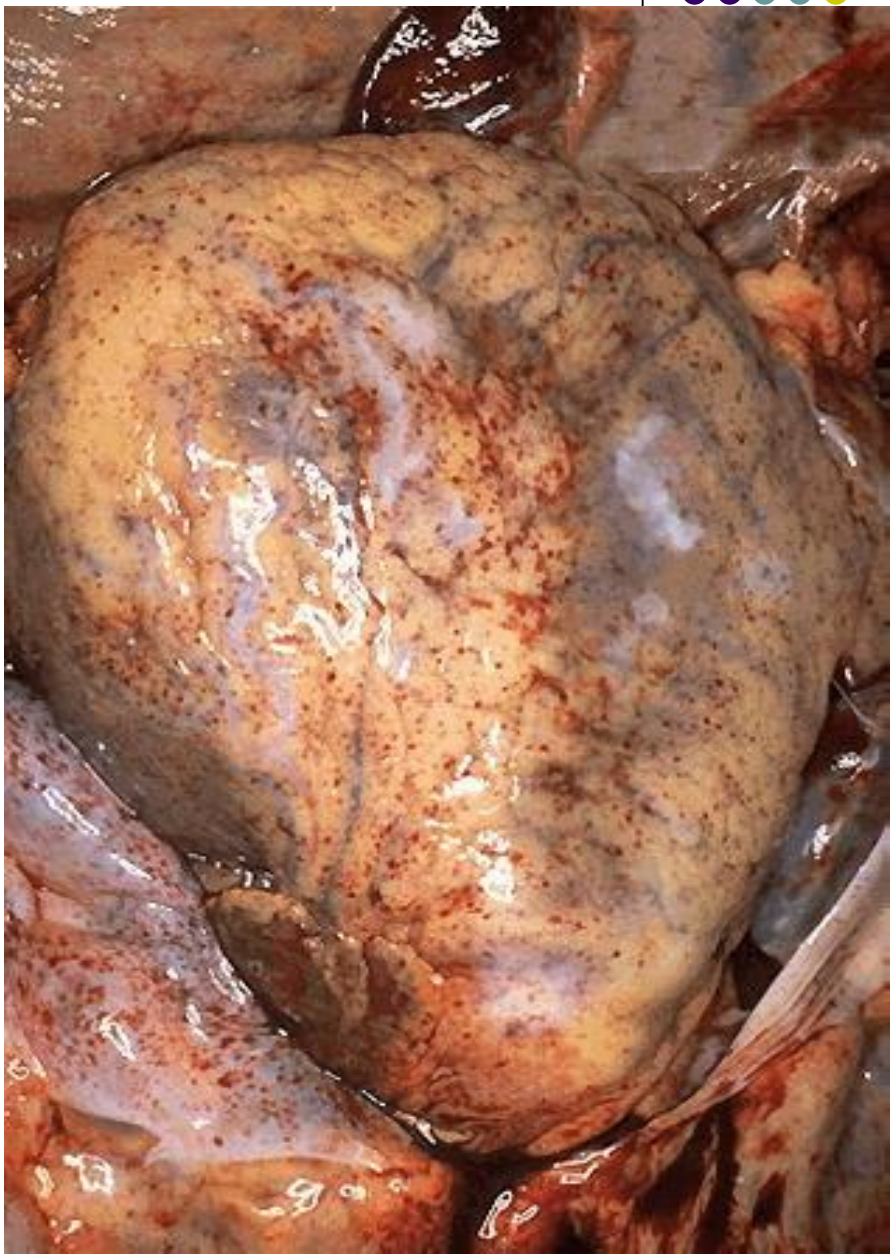
due to ruptured aortic aneurysm

→ fatal

Hemorrhage

2) *Petechiae:*

minute hemorrhages into skin, mucous membranes, or serosal surfaces (1-2 mm)



- **Associated with:**
  - Local increase hydrostatic pressure
  - Thrombocytopenia
  - Defective platelets function
  - Defective clotting

Hemorrhage

3) Purpura:

- Slightly larger hemorrhages than petechiae,
- measures (3-5 mm)
- ***Causes:***
  - Causes as petechiae
  - Trauma
  - Vasculitis
  - Increased vascular fragility

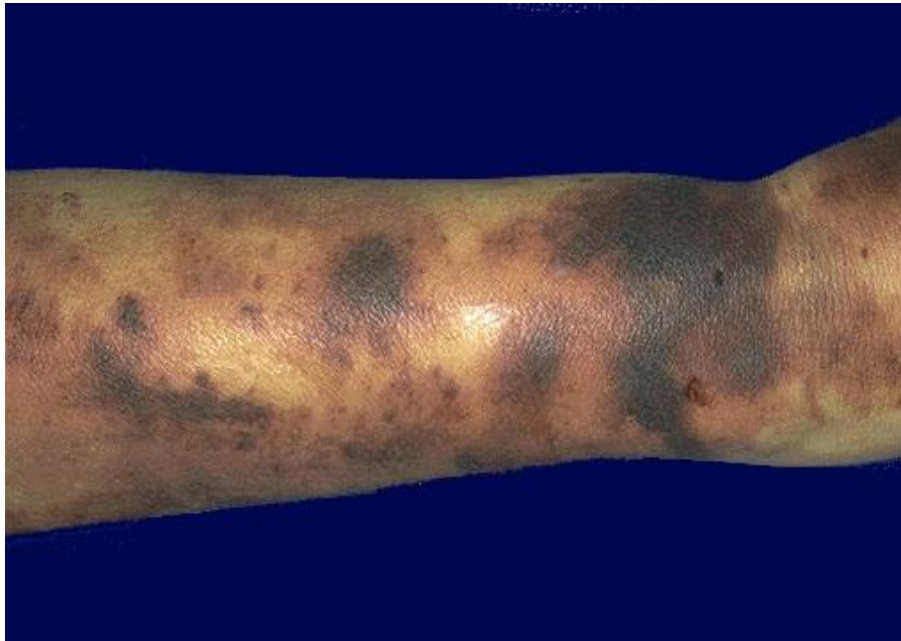
Hemorrhage

4) Ecchymoses:

- Subcutaneous hematoma ‘bruise’ over 1-2 cm

Q: Why do **bruises change color** as they Resolve?

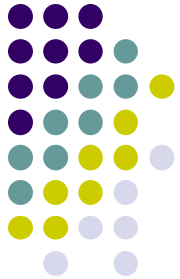
- The RBC’s in a hemorrhage are broken down:
  - hemoglobin (red) →
  - bilirubin (blue-green) →
  - hemosiderin (golden-brown)



Hemorrhage

- **Accumulation of blood in a body cavity:**
  - Hemothorax
  - Hemopericardium
  - Hemoperitoneum
  - Hemarthrosis

Clinical Effects of Hemorrhage



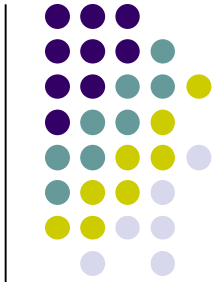
- **< 20%** blood loss, in otherwise **healthy individuals** →

  little health effect

  - That's why donating blood is OK

- **> 20%** blood loss → **Hemorrhagic Shock**

Clinical Effects of Hemorrhage



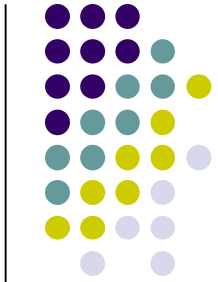
- **Patient Condition:**
  - But in patients who have **heart or lung disease** →

even **mild blood loss** could decrease critical oxygen carrying capacity →

'heart attack'

- **Site** → **Bleeding into the brainstem is fatal** while same blood loss from a finger cut is trivial

Clinical Effects of Hemorrhage



- **Chronic** recurrent bleeding
  - (e.g. peptic ulcer, menstrual bleeding) → can lead to

    iron deficiency anemia!

- Anemia from Blood Loss:
  - This may be the only hint of Occult Cancer
    - Carcinoma of the Colon
    - Gastric Carcinoma (less common)

Hemodynamic Disorders, Thrombosis & Shock

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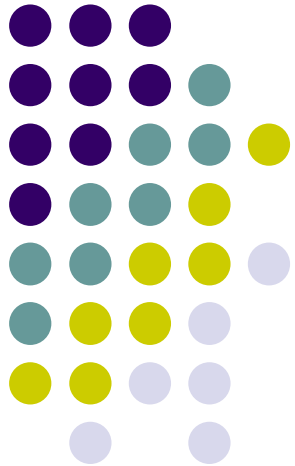
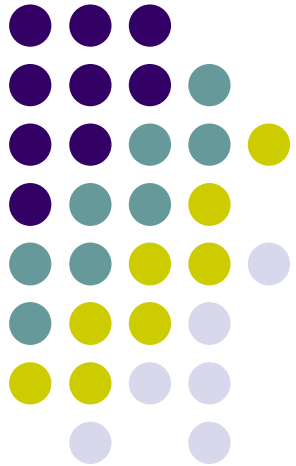
- Edema
- Hyperemia and Congestion
- Shock



Hyperemia & Congestion



Increased blood in an area

(inside blood vessels)

compared to normal

Compare between:

"Hyperemia & Congestion"

Hyperemia:

- is an "active process"
- resulting from augmented tissue inflow
- due to arteriolar dilation
- (e.g. acute inflammation)

Congestion

- is a "passive process"
- resulting from impaired outflows from a tissue
- Impaired venous return
- (e.g. cardiac failure or venous obstruction)

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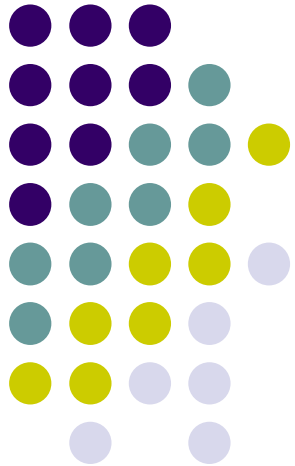
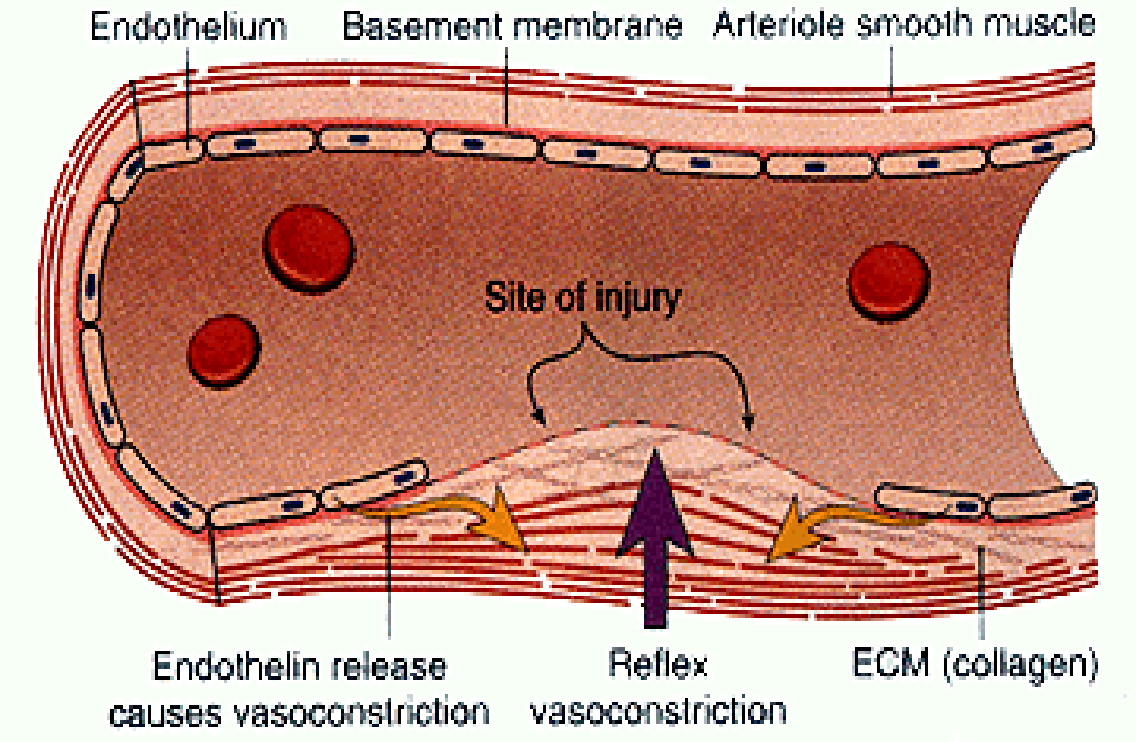


Hemostasis

- after initial injury (e.g. a small cut) → there is a brief period of arteriolar vasoconstriction (neurogenic reflex mediated by **endothelin**)

A transient effect

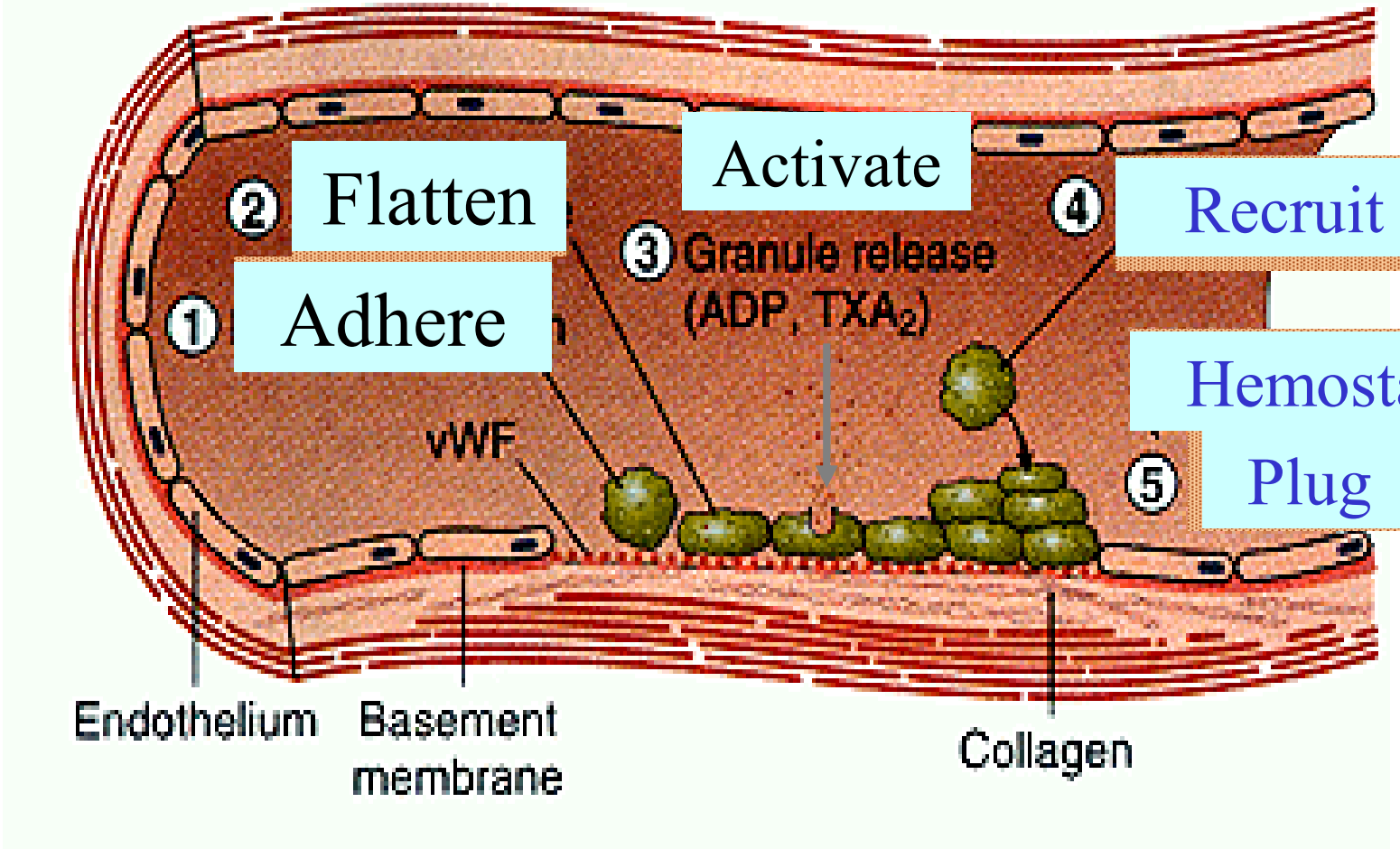
Vasoconstriction



Hemostasis

- Endothelial injury exposes the blood to the extracellular matrix (ECM)
  - The ECM is highly thrombogenic
  - Platelets adhere, flatten and then activate
  - To form hemostatic plug **(primary hemostasis)**

Primary Hemostasis

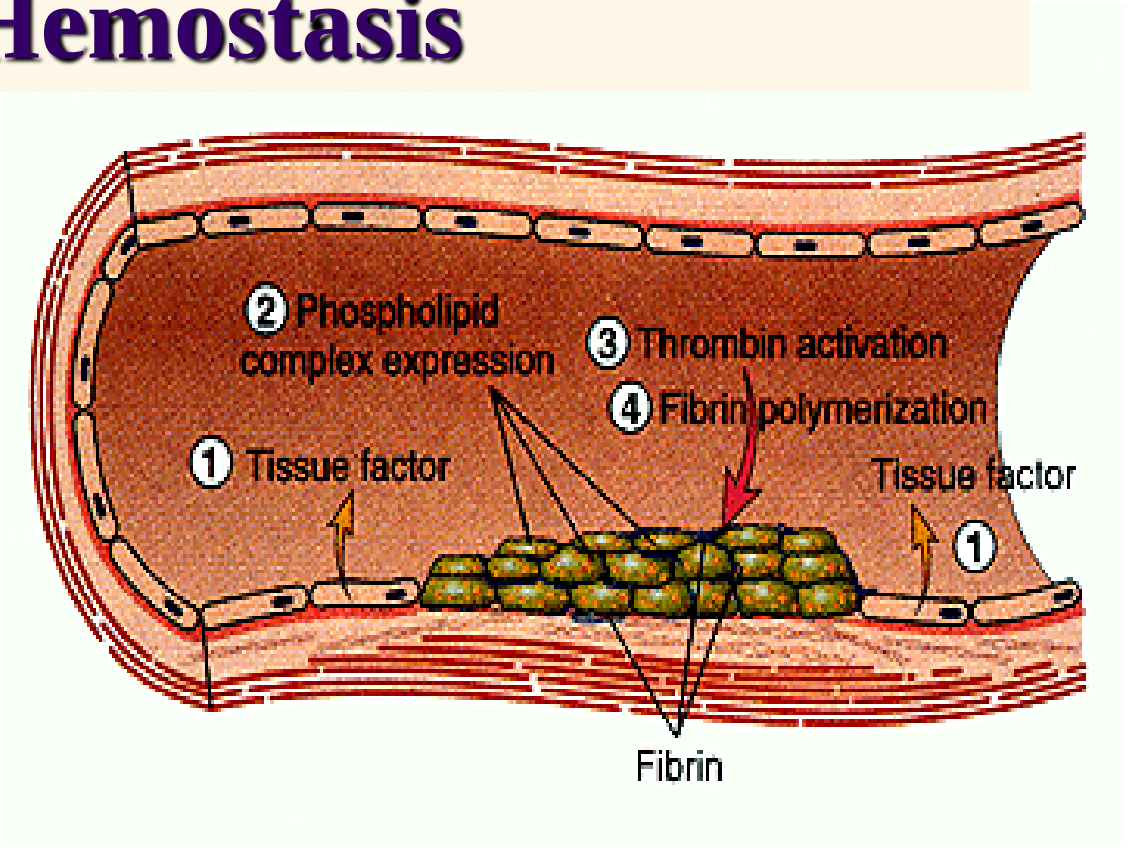


vWF = von Willebrand Factor

Secondary Hemostasis

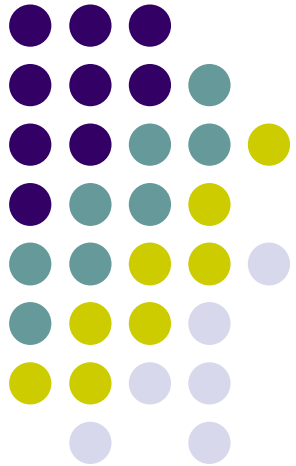
- tissue factor together from endothelial cells & platelet factors activate the ***coagulation cascade with fibrin deposition***
- Thrombin activation induces further platelet recruitment and granule release (secondary hemostasis)
- polymerized fibrin and platelets aggregate to form permanent plug

Secondary Hemostasis



Thrombosis

- The formation of a blood clot **(thrombus)** **within the non-interrupted vascular system**
- due to inappropriate activation of normal hemostatic processes



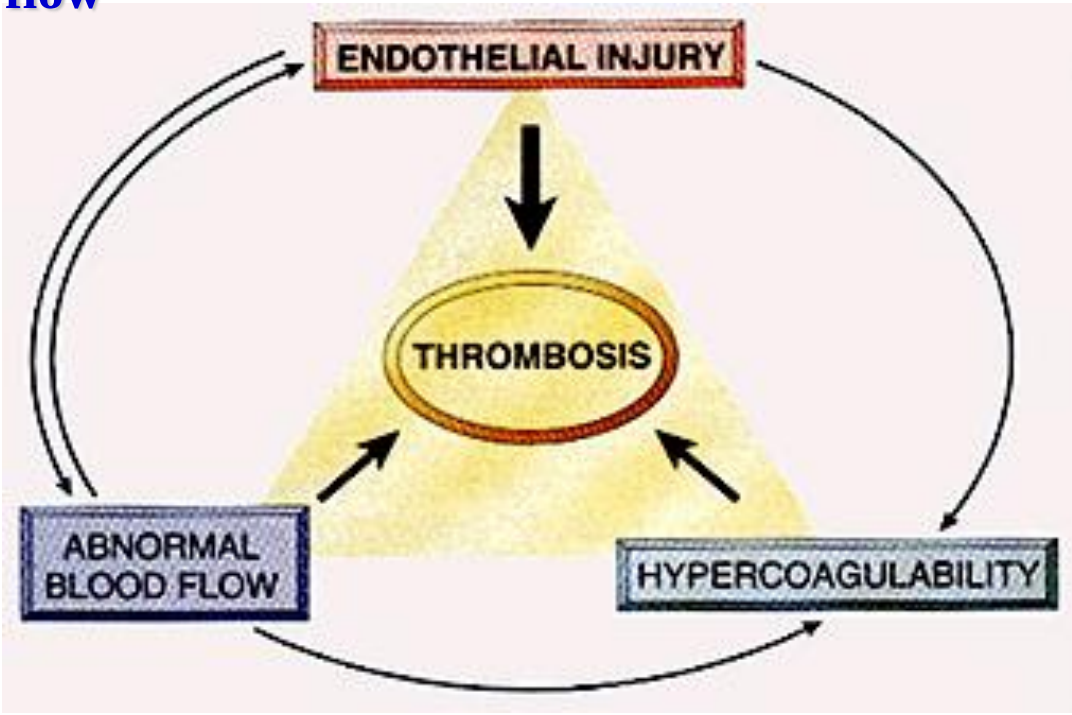
Thrombosis

Pathogenesis:

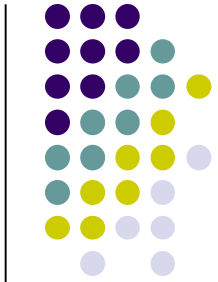
Predisposing Factors:

Virchow's Triad:

1. **endothelial injury**
2. **stasis or turbulence of blood flow**
3. **blood hypercoagulability**



1) Endothelial Injury



- Important for thrombus formation in the heart and arterial circulation →

Causes:

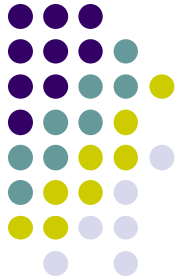
1. **Endocardial injury (myocardial infarction, valvulitis)**
2. **Severe Atherosclerosis**
3. Hypertension
4. Bacterial endotoxins
5. Hyperchlosteremia, homocystinuria, radiation
6. Toxic Products (Cigarettes)

2) Abnormal Blood Flow

Causes:

- Predisposing conditions in Arteries and the Heart:
  1. **Atherosclerosis**
  2. **Aneurysms**
  3. **Myocardial Infarction**
  4. **Heart Valves abnormalities**
  5. **Heart chambers dilation**
  6. **Atrial dilatation & fibrillation**
  7. Hyperviscosity Syndromes e.g. (Sickle cell anemia, Polycythemia)

2) Abnormal Blood Flow



Turbulence & Stasis → Thrombosis

HOW???

1. Disrupt normal laminar flow and bring **platelets in contact with endothelium**
2. Prevent dilution of **activated clotting factors**
3. Retard the inflow of **clotting factor inhibitors** → Permit thrombi build-up
4. Promote **endothelial cell activation**

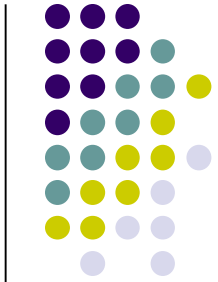
3) Hypercoagulability

- Any alterations of the coagulation pathways that predispose to thrombosis:
  - **Primary (genetic)**

    or
  - **Secondary (acquired) disorders**

3) Hypercoagulability:

Primary - Genetic



A) Mutation of Factor V Gene

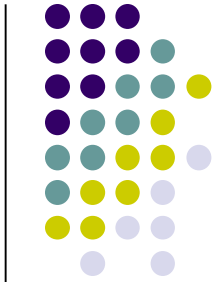
Factor V mutation "Leiden Mutation":

B) Mutation of Prothrombin gene

C) Inherited Lack of Other Anticoagulants

3) Hypercoagulability:

Secondary - Acquired



1. **Cardiac failure:**
   - multifactorial
2. **Oral Contraceptives & Hyperestrogenic state of pregnancy:**
   - (due to increased hepatic synthesis of coagulation factors & reduced synthesis of antithrombin III)
3. **Disseminated cancer:**
   - (due to procoagulant tumour products)
4. **Advancing age:**
   - (due to increase platelet aggregation & reduced PGI2 by endothelium)
5. **Smoking & Obesity**

Morphology of Thrombi

- **Thrombi Develop**

  INSIDE THE CARDIOVASCULAR SYSTEM

- {BUT, bleeding into the peritoneal area, for example, forms:

  a blood clot - NOT a thrombus}

Morphology of Thrombi

- **Lines of Zahn**
  - Alternating **pale layers of platelets & fibrin with darker layers of RBC's**
  - Imply formation in areas of **active blood flow** such as in the heart, aorta or larger arteries
  - Venous thrombi form in a more sluggish flow zone and often lack lines of zahn

Clinical Correlations:

Venous Thrombosis

1) Superficial Veins of the Lower Extremities

- Cause pain, swelling
- **rarely embolize**
- Associated with varicosities
  - Varicose veins - abnormally dilated, tortuous veins
- Increased risk of infections
- Increased risk of varicose ulcers

Clinical Correlations:

Venous Thrombosis

2) Thrombi in Deep Veins

- **(Popliteal, femoral, iliac veins)**
- **more likely to embolize ----**
- May produce edema, pain and tenderness
- About 50% are asymptomatic (due to formation of collaterals)

Clinical Correlations:

Venous Thrombosis

2) Thrombi in Deep Veins --- Predisposing Factors:

- Cardiac Failure (CHF)
- **Reduced physical activity:**
  - Trauma
  - Surgery
  - Burns
  - Bed rest and immobilization
- 3rd term Pregnancy & Postpartum
- Disseminated cancers:
  - Migratory Thrombophlebitis (Trousseau's Syndrome)

Clinical Correlation

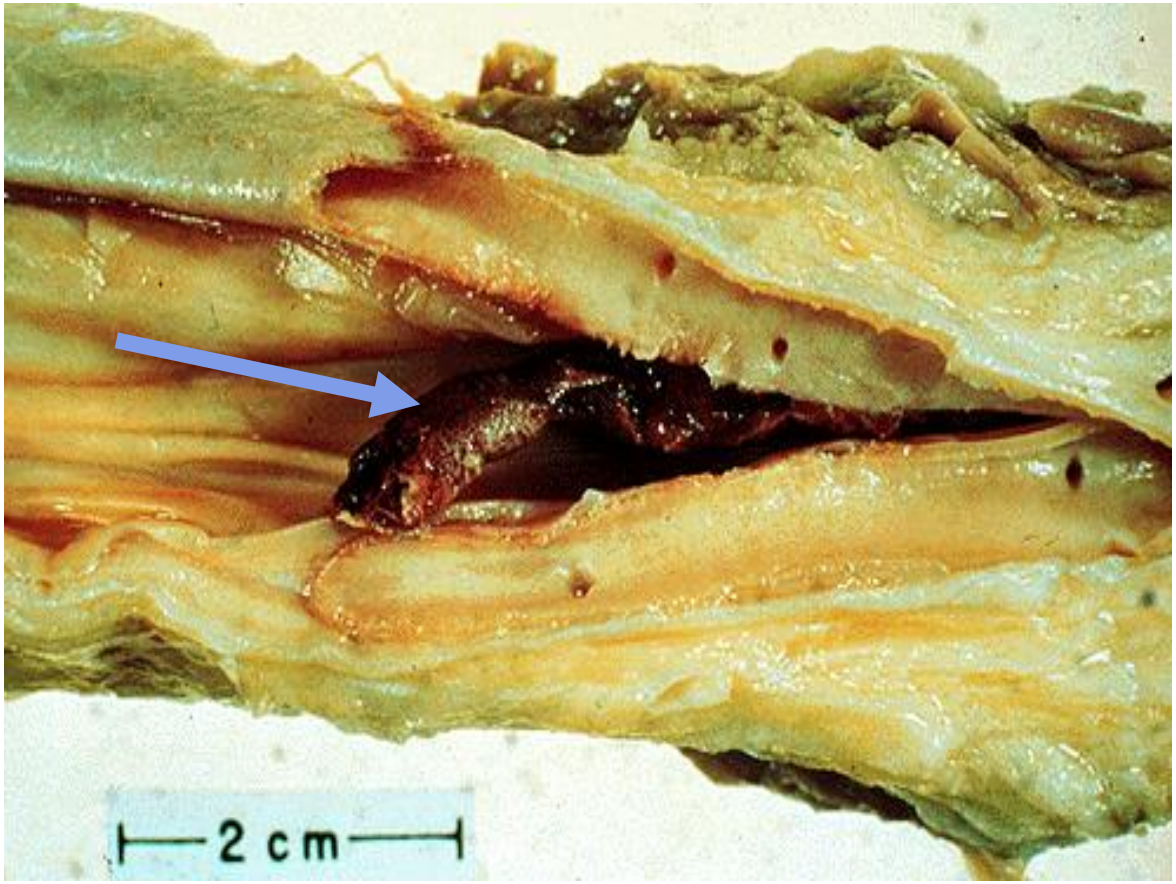
- Thrombi are significant because:
  1. They cause **Obstruction**
  2. They **Embolize**

Fate of Thrombosis

1. **Propagation and obstruction**
2. **Embolization**
3. **Dissolution “nothing left”**
4. **Organization and recanalization**

1) Propagation

- Thrombus accumulate more platelets and fibrin → gets larger
- Leading to obstruction



2) Embolism

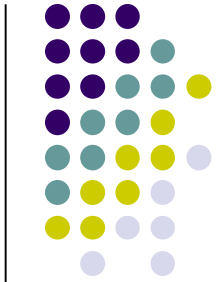
- Fragmentation and dislodge of a thrombus

  transported by the blood in the vasculture to a site

  distant from its point of origin

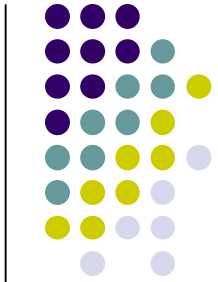
  - → (to be discussed later)

3) Dissolution of Thrombi



- Activation of fibrinolytic system
- Recent thrombi can undergo total lysis
- Older thrombi won't undergo lysis (due to extensive fibrin polymerization)
  - Thus the use of t-PA(tissue plasminogen activator) is only effective in the first 1-3 hours

4) Organization / Recanalization



- Granulation tissue followed by:
  - Capillary channel formation → re-establishing the flow

    "recanalization"
  - May ***heal*** so totally as to leave only a small fibrous

    'lump' as evidence of a previous thrombus

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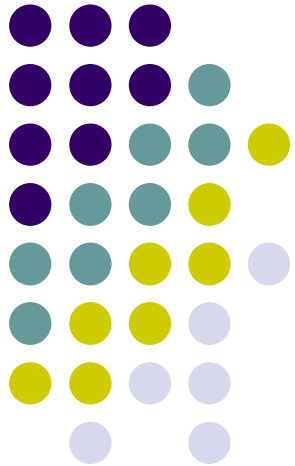
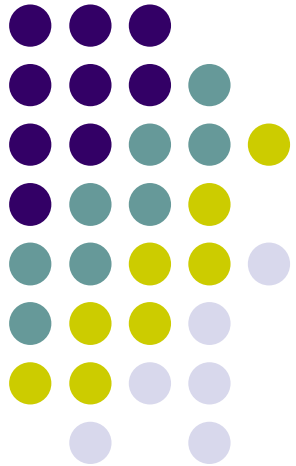


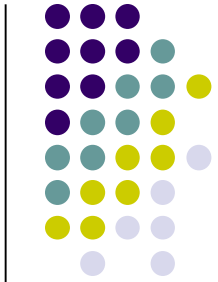
Embolism

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



Embolism



Source:

- 99% are dislodged thrombus:
  - ***thromboembolism***
- Rarely:
  - fat, air, atherosclerotic debris, tumor fragments, bone marrow, foreign bodies (bullets)

Embolism

Potential consequence:

- ischemic necrosis (infarction)

Embolism

- ***Potential Consequences:***

Ischemic necrosis (infarction)

1. Though **pulmonary emboli are common** and important,
   - secondary pulmonary infarction is not common
   - Lung is protected by a dual blood supply
2. **The brain is not so protected** and gets infarcts (stroke)

LIQUEFACTIVE NECROSIS

Pulmonary Thromboembolism

- Generally originate from

  deep leg veins (in 95%)

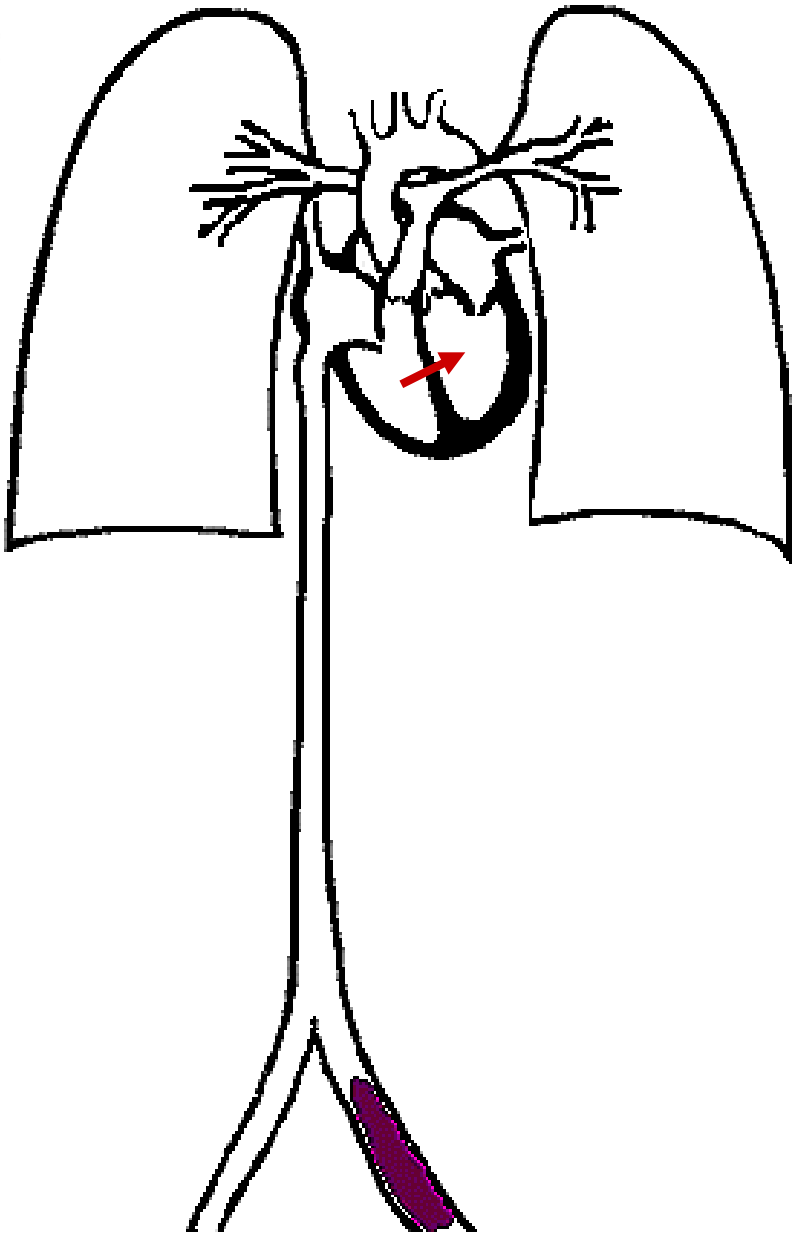
- Usually pass through the right heart into **pulmonary vasculature**

- **What is "paradoxical embolism"??**

  - an embolus from deep veins →

  pass through an interarterial or

  interventricular **defect** → to gain access to the systemic circulation



Pulmonary Thromboembolism

- ***Effects:***

May occlude:

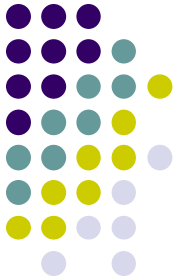
- **main** pulmonary artery, across the bifurcation **(saddle embolus)**
- or pass into the **smaller**, branching arterioles
- **multiple** emboli may occur

Pulmonary Thromboembolism

Clinical Effects:

1. **Small size** emboli (in 60-80% of cases) → ***Clinically Silent***
2. If obstruct > **60% pulmonary circulation** → Sudden Death / OR Right heart failure *(core pulmonale)*
3. Emboli **in medium-sized arteries** may result in → hemorrhage **without infarction**
4. if bronchial circulation is **compromised** (as in left heart failure) → infarction
5. Multiple PE → **pulmonary hypertension** & right heart failure
6. Initial PE increases the risk for → more PE!

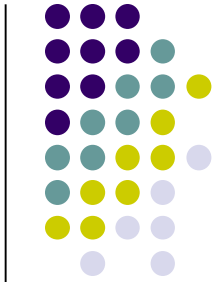
Systemic Thromboembolism



"Emboli traveling within the arterial circulation"

- 80% arise from **intracardiac mural thrombi**

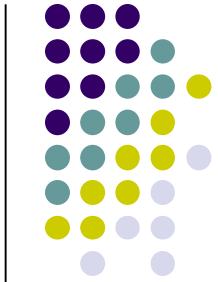
Systemic Thromboembolism



Causes:

- ***Thrombi formed on:***
  - Myocardial infarction - left ventricle
  - Dilated left atrium - due to mitral valve abnormalities
  - Atherosclerosis Aorta
  - Aortic aneurysm
  - Valvular vegetations (thrombi)
  - Paradoxical thrombus (uncommon)

Systemic Thromboembolism



- ***Effects:***
  - Emboli traveling within the **arterial circulation *to a wide variety of sites:***
    - ***Lower extremities (75%)***
    - ***Brain (10%)***
    - ***Intestine, spleen, kidney (less frequent)***
  - Lead to **infarction** in the distribution of obstructed vessel

Fat Embolism

Microscopic **fat** globules in the circulation

derived from:

- long bone fractures (fatty marrow)
- or soft tissue trauma and burns (rarely)

- < 10% of cases show clinical findings: →

fat embolism syndrome

Fat Embolism

Fat Embolism Syndrome:

- ***Characterized by:***

1. Pulmonary insufficiency
2. Neurologic symptoms
3. Anemia
4. Thrombocytopenia

- Only 10% of these cases are fatal

Air Embolism

Gas bubbles within the circulation can obstruct vascular flow to cause distal ischemic injury

- ***Causes:***
  1. Obstetric procedures
  2. Chest wall injury
  3. Sudden atmospheric pressure changes (decompression sickness → e.g. divers)
- ***Effects: (> 100 mL of air)***

Amniotic Fluid Embolism

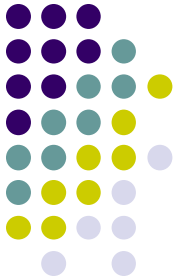
Infusion of amniotic fluid into maternal venous circulation

Causes:

1. Torn placental membrane - amniotic fluid release
2. Rupture of uterine veins

- *Mortality of 80%*

Disseminated Intravascular Coagulation (DIC)



- **Sudden widespread fibrin deposition in microcirculation**
- Rapid consumption of platelets and coagulation proteins ***(consumption coagulopathy)***
- **Secondary massive fibrinolysis**, all the little thrombi dissolve
- Clotting disorder turns into a **Bleeding Disaster**

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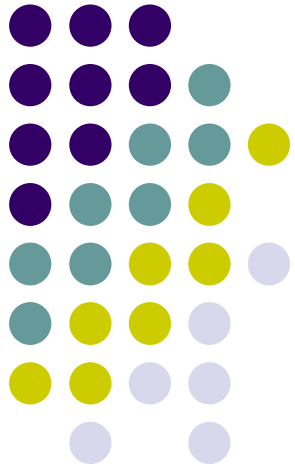
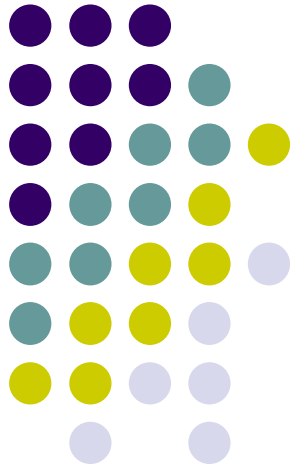


Infarction

An area of ischemic necrosis caused by occlusion of either the arterial supply or the venous drainage in a particular tissue



Infarction

- ***Causes:***

1. Arterial occlusion due to **thrombotic or embolic** events (99%)
2. **Other arterial** causes:
   - Vasospasm
   - Swelling of atheroma
   - Extrinsic compression on vessel (by tumor …)
   - Twisting of vessels
   - Traumatic rupture
3. **Venous thrombosis**:

   in organs with single venous outflow e.g. testis, ovary

Infarction

Morphology:

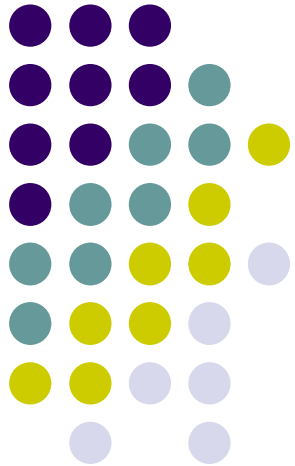
- ***White infarcts***: - (arterial occlusion, solid organs)
- ***Red infarcts***: - (venous occlusion, loose tissue, dual circulation, congested tissue, reperfusion)

Infarction

- **Factors that influence Development of an infarct**
  - Nature of the vascular supply (dual arterial supply)
  - Rate of development of occlusion
  - Vulnerability of the tissue to hypoxia
  - Oxygen content of blood

Hemodynamic Disorders, Thrombosis & Shock

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



Shock

Systemic hypoperfusion due to reduction either in:

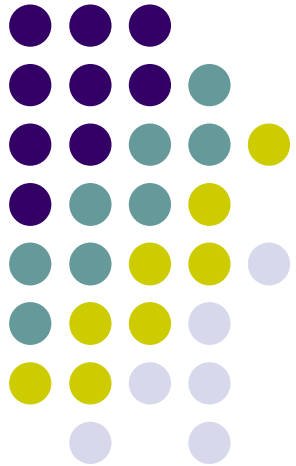
- **cardiac output**
- or in the **effective circulating blood volume**

results are:

Hypotension, followed by

Impaired Tissue Perfusion and

Cellular Hypoxia



Shock

- Shock or “cardiovascular collapse” is the final common path for a diverse group of lethal events:
- Three Main Categories:
  1. **Cardiogenic**
  2. **Hypovolemic**
  3. **Septic**
- Others:
  4. Neurogenic Shock (spinal cord injury)
  5. Anaphylactic Shock

1) Cardiogenic Shock

Results from **Severe Myocardial Pump Failure**

Due to:

- Myocardial Infarction
- Ventricular Arrhythmia
- Extrinsic Compression (Cardiac Tamponade)
- Outflow Obstruction (Pulmonary Embolism)

2) Hypovolemic Shock

Results from **Loss of Blood or Plasma Volume:**

- Hemorrhage
- Fluid loss from severe burns or trauma

3) Septic Shock

- Caused by systemic microbial infection
- Dissemination of infection into the vasculature
- Most often caused by "*endotoxin-producing* gram-negative" infection (endotoxic shock)
- But can also occur with gram-positive and fungal infections
- Most common cause of death in ICU's in the US