**Circulatory disturbances**

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**Objectives:**
Recognize and describe different forms of circulatory disturbances as edema, hemorrhage, thrombosis, embolism, ischemia, infarction, congestion, gangrene and shock.

**Edema**
Edema is abnormal accumulation of fluid in the interstitial tissue or body cavities.

- **Causes of edema**

  **Increased Hydrostatic Pressure**
  - Impaired venous return
  - Congestive heart failure
  - Constrictive pericarditis
  - Ascites (liver cirrhosis)
  - Venous obstruction or compression
  - Thrombosis
    - External pressure (e.g., mass)
    - Lower extremity inactivity with prolonged dependency
  - Arteriolar dilation
  - Heat
  - Neurohumoral dysregulation

  **Reduced Plasma Osmotic Pressure (Hyproproteineimia)**
  - Protein-losing glomerulopathies (nephrotic syndrome)
  - Liver cirrhosis (ascites)
  - Malnutrition
  - Protein-losing gastroenteropathy

- **Distribution of edema**
It may be generalized or localized only to one part of the body.

  **Generalized**
  - Cardiac
  - Renal
  - Hypoproteinemia

  **Localized**
  - Inflammatory
  - Lymphatic obstruction
  - Local venous obstruction

**What is the special distribution of each type of edema?**
- **Cardiac** :
  - Gravitational edema, later on generalized.
- Renal:-
  a. Nephretic: Peri-orbital then generalized. Mild to moderate
  b. Nephrotic: Generalized, usually massive.
- Nutritional: Generalized

**Most important organs affected by edema**

- 1- Subcutaneous tissue......most common site
- 2- Lung......in left sided heart failure......dyspnea
- 3- Brain......local or generalized.....headache and may be brain herniation.

![Image](image.png)

**Pitting and non pitting edema**

- In pitting edema, fluid escapes in tissue spaces on pressure.
- Cardiac, renal, nutritional and edema due to venous obstruction are all pitting edema

**What are the causes of non pitting edema?**

- a. Inflammatory edema .. due to the presence of fibrin in inflammatory exudates.
- b. Edema due to lymphatic obstruction... rupture of lymphatics and escape of lymph in the interstitial tissue initiates fibrosis.

**About edema.....**

- Edema fluid is a transudate except......... (inflammatory edema..exudate)
- Anasarca is.... Generalized edema + effusion of the serous sacs
- Hydrothorax is.....
- Hydro pericardium is...
- Hydroperitonium (ascitis) is.....
- Hydrocele
- Hydroarthrosis is.....
- Edema due to lymphatic obstruction is called...... lymphoedema
**Hyperemia and congestion**
- Both terms hyperemia and congestion mean a local increased volume of blood in a particular tissue.
- **Active hyperemia** denotes increased flow in an area due to arteriolar dilatation e.g. - Acute inflammation. - Muscle exercise. - Blushing of the face.
- The affected organ is **red** due to engorgement with oxygenated blood.

**Congestion**
- Is a passive type of hyperemia due to obstructed venous flow or increased back pressure from congestive (right sided) heart failure.
- **Acute congestion**
  - Sudden right sided heart failure. - Shock.
- **Chronic congestion**
  - Localized....pulmonary congestion in left sided heart failure.
  - Generalized....all organs (including liver) in right sided heart failure.
  - Affected organ is **blue red** in color due to increased non-oxygenated blood.

**Chronic venous congestion of the liver**
- In most cases it is part of generalized congestion caused by right sided heart failure.
- During the early stages, the central part of hepatic lobule is affected with dilated central vein and adjacent blood sinusoids... deep red color.
  - The mid zone of the lobule suffer hypoxia and shows fatty change.....yellow color.
  - The alternating red and yellow color resemble the nutmeg seed.

**Is it a true type of cirrhosis?**
Chronic venous congestion (lung)

- It is caused most often by
  - Left sided heart failure.
  - Mitral stenosis.
- Congestion and distention of alveolar capillaries leads to transudation of fluid into alveolar spaces, rupture of capillaries leads to passage of RBSs into the alveoli.
- At this stage the lungs are enlarged, heavy, blush-red in color and C/S oozes bloody froth.

Heart failure cells

- Phagocytosis and degradation of red cells result in intra-alveolar hemosidrin-laden macrophages called **Heart failure cells**.
- In long standing congestion, fibrosis of interstitium and hemosidrin deposition results in **Brown induration** of the lung.
- At this stage the lung appears dark brown with firm consistency (indurated) due to associated fibrosis.

**Define Heart failure cells and Brown induration of the lung**

Hemorrhage

- It means escape of blood outside the cardiovascular system.
- Causes may be
  - local....trauma, inflammation, erosion of blood vessel by tumor.
  - General...bleeding tendencies, hypertension, anticoagulant therapy
- According to its site it may be
  1- Interstitial....in tissue spaces.
  2- Internal.......In serous sacs.
  3- External......Outside the body.

1- **Interstitial Hemorrhage**

- Accumulation of blood within tissues is called **hematoma**. According to the size of hematoma it is called:-
A- Petechia...1-2 mm in diameter. Found in the skin, m.m, or serosal surfaces.

- Causes:
  * Increased intracapillary pressure.
  * Low platelet count (thrombocytopenia).
  * Defective platelet functions (uremia).
  * Clotting factor defects.

Petecheal hemorrhages of the pericardium and brain

B- Purpura

- Larger hematomas ...more than 3 mm in diameter.
- Can be caused by the same causes of petechial hematomas.
- Can be caused also by increased vascular fragility e.g. by vasculitis or amyloidosis.

Purpuric bleeding

C- Ecchymosis

- Larger subcutaneous hematomas (1-2 cm. in diameter).
- Usually seen after traumas but can be caused by any of the previous conditions.
- Characteristic color changes occur in it
  - Red-blue...blue-green ...golden brown.

Ecchymosis
2- Internal hemorrhage
- It is hemorrhage inside body cavities.
  - Hemothorax....... Hemorrhage into pleura
  - Hemopericardium.... Hemorrhage into the pericardium.
  - Hemoperitoneum.... Hemorrhage into peritoneal sac.
  - Hematocoel....... Hemorrhage into tunica vaginalis of the testis.
  - Hemarthrosis...... hemorrhage into joint space.

3- External hemorrhage
- It is hemorrhage through body orifices.
  - What is meant by each of the following terms
    - Epistaxis  - Hemoptysis  - Hematemesis  - Melena
    - Bleeding per rectum (hematochezia)
    - Hematuria  - Menorrhagia  - Metrorrhagia
  - Clinical significance of hemorrhage
    - Depends upon amount, rate and site of hemorrhage.
    - Acute or chronic loss of 20% of total blood volume does not affect healthy individuals.
    - Acute loss of more than 25% of blood volume produce hypovolemic shock.
    - Chronic external blood loss induce iron deficiency anemia while chronic internal blood loss does not. Why??
    - Large subcutaneous hematoma may not be harmful while a small brain hematoma can be fatal.

Hemostasis And Thrombosis
- Hemostasis:
  Is a physiological process designed to stop bleeding from ruptured blood vessel.
- Thrombosis:
  Is a pathological process resulting in coagulation of blood inside intact blood vessel.
- Both processes depend upon the interaction of three components:-
1- Endothelium

- Has both anticoagulant and procoagulant functions according to the body needs.
- **Anticoagulant factors of endothelium:**
  1- Inhibition of platelet aggregation by secretion of prostacyclin(PGI2), ADP and NO. VD...increase blood flow...decrease platelet adhesion to vessel wall.
  2- Anti-thrombin activity mediated by thrombomodulin.
  3- Fibrinolysis through the secretion of plasminogen activator...++plasmin...lyses of fibrin....prevents the growth of the clot.
- **Procoagulant factors of endothelium:**
  Through the release of
  1- vonWillebrand factor from Weibel-palad granules in the cytoplasm...+++binding of platelets to surfaces and it is a carrier of factor VIII.
  2- Thromboplastin (tissue factor III).....++extrinsic pathway of coagulation cascade.
  3- Inhibitor of plasminogen activator (PAI)....... inhibit fibrinolysis.

2- Platelets

- **Platelet functions:**
  1- Maintain the physical integrity of the vascular endothelium.
  2- Secretion of PDGF which promotes endothelial repair.
  3- Form platelet plug.
  4- Promote coagulation cascade through platelet phospholipids complex.
2- Platelet reactions

- **These include:**
  1- Adhesion
  2- Release reaction.
  3- Activation of coagulation cascade.
  4- Arachidonic acid metabolism.
  5- Platelet aggregation.
  6- Stabilization of platelet plug.
  7- Limitation of platelet plug formation

Normal hemostasis, platelet functions

- A- After vascular injury, local neurohumoral factors produce transient vasoconstriction.
- B- Platelets **adhere** to exposed ECM via (vWF) and are activated resulting in **shape** changes and **release** of (ADP & TXA2).... Platelet **aggregation** to form the primary hemostatic plug

- C- Local activation of coagulation cascade results in fibrin polymerizations and firm adhesion of platelets forming secondary plug.
- D- Limitation of platelet plug formation by tissue plasminogen activator, antithrombins, proteins C and S. These act to prevent uncontrolled enlargement of thrombus

3- Coagulation cascade

- Described in two distinct but interconnected pathways.
  - An **intrinsic** and **extrinsic** pathways
**Thrombosis**

It is the process of thrombus formation.

**Thrombus**

It is a compact mass formed of the circulating blood elements within the cardiovascular system during life.

**Predisposing factors for thrombosis:**

Three main factors (Virchow's triad)

1. **Endothelial damage (dysfunction).**
2. **Change in the pattern of blood flow (stasis or turbulence).**
3. **Changes in composition of blood (blood coagulability).**

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**Virchow's triad**

1. **Endothelial damage (dysfunction)**

<table>
<thead>
<tr>
<th>Causes</th>
<th>Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>B- Atherosclerosis.</td>
<td>..... Decrease production of anticoagulants (thrombomodulin, antithrombin III, NO, PA).</td>
</tr>
<tr>
<td>C- Infections (thrombophlibitis).</td>
<td>B- Endothelial loss ...exposure of underlying ECM ..... ++ of platelet adhesions by vWF ...formation of platelet aggregates and ++ coagulation cascade</td>
</tr>
<tr>
<td>D- Autoimmune disease (PAN).</td>
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<tr>
<td>E- Trauma or surgery.</td>
<td></td>
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<tr>
<td>F- Metabolic disease (hyperlipidemia)</td>
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</tbody>
</table>

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2- Change in the pattern of blood flow (stasis or turbulence).

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</table>
| **A- Stasis** occurs mostly in **veins**  
Caused by venous obstruction  
-From inside….thrombus  
-From outside…pressure by tumor,L.N  
-From the wall…ligature, spasm.  

**B- Turbulence** occurs mostly in  
- **arteries**….aneurysms  
- **heart**….dilated cardiac chambers that do not contract properly (atrial fibrillation)  

| A- Stasis….1- Reduces the inflow of fresh blood that contain natural anticoagulants.  
2- Retard the removal of small platelet aggregates.  

| B- Turbulence… mechanically injure endothelial cells.  

| C- **Stasis and turbulence**….  
1- activate the secretion of procoagulant factors.  
2- bring platelets and leucocytes in contact with the endothelium (loss of laminar flow) and facilitate their attachment. |

3- Changes in composition of blood (blood coagulability).

- Increased concentration of coagulation proteins or reduced concentration of natural anticoagulants. This change may be hereditary, acquired or immune mediated

**A- Hereditary:** -
* About 5-10% of all people have some genetic defect predisposing them to thrombosis.  
* These include congenital deficiency of antithrombin III, protein C and protein S and mutation in the gene encoding factor V.

**B- Acquired :**-
* Tissue damage….increase the production of thromboplastin and other procoagulants.  
* Chronic infection…. Liver produces excess fibrinogen (one of acute phase reactants).  
* Estrogen containing oral contraceptives….increase the production of prothrombin and fibrinogen.  
* Shock……. Increased incidence of DIC.  
* Tumors…..increased release of thromboplastin.

**C- Immune mediated thrombosis**
* Anti-phospholipid antibodies…released during strokes or infarction……. Antibodies are formed which bind with phospholipids of platelets promoting their aggregation and destruction.
*Heparin-induced thrombocytopenia......seen in 5% of patients with chronic use of high molecular weight heparin.
- Caused by antibodies to the complex of heparin and platelet factor 4.... Antibodies cross reacts with platelets and endothelial cells......platelet and endothelial injury ..........thrombosis.
* Poly arteritis nodosa (PAN) and systemic lupus erythematosus (SLE)

**D**- Disseminated intravascular coagulation. (DIC).

- It is a clotting disorder characterized formation of thrombi in small blood vessels (arterioles, capillaries and venules). Formation of these microthrombi consumes the platelets (resulting in thrombocytopenia) and other coagulation proteins. This leads to bleeding which cannot be stopped easily.

**Causes of DIC:-**
- 1-Infections.....by gram negative sepsis, fungal infection....
- 2- Neoplasma......especially of the GIT.
- 3- Massive tissue injury....trauma ,burns, extensive surgery.
- 4- Shock.
- 5- Obstetric complications...amniotic fluid embolism, eclampsia, and abruption placentae.

**Morphology of thrombi**

Large thrombi formed in veins, arteries and heart of living patients have typical features that distinguish them from postmortem clots. These include

1- **Lines of Zhan**: Formed by deposition of platelets and fibrin, which form a white layer. RBCs deposit on this layer forming a red layer on which a new layer of fibrin and platelets is deposited. These alternating white and red lines are called lines of Zhan.

2- **Friability** :- Thrombi are held together with fibrin that does not permeate all layers uniformly but leaves cleavage lines between the white and red layers. The friability of thrombi accounts for the fact that they may detach and embolize.
3- **Attachment**: Thrombi are attached to the surface of the vessel or heart chamber in which they arise.

4- **Molding**: Thrombi formed inside veins typically retain the shape of the vessel in which they originate. They fill and expand the affected vessel and its tributaries.

*Postmortem clots:*

They differ from thrombi in that

1- They form in stagnant (non-circulating) blood.
2- Red blood cells sediment and separate from plasma forming (red current jelly) the plasma above forms a yellow part (chicken fat). No lines of Zhan are formed.
3- They are not attached to the wall of blood vessel and can be washed easily from it.
4- They are soft and moist (not friable).
5- They do not fill or expand the affected vessel.

**Sites of thrombi**

Thrombi that occur in different parts of the circulation have different causative factors and different macroscopic appearances.

1- Arterial and cardiac thrombi: (Pale thrombi)

- Form in fast moving blood.
- Have prominent laminations.
- Have relatively high platelet/fibrin content and therefore they are firm, pale, attached firmly to the wall (mural thrombi).
- Their obstructive effects are more dangerous than embolic.
2- Venous thrombi “phlebothrombosis” (red thrombi)

- Form in slow-moving blood.
- Have a high proportion of trapped red cells in relation to platelet/fibrin therefore they are red, soft gelatinous with poor lamination.
- They grow (propagate) towards the direction of the heart.
- Their embolic effects are more dangerous than their obstructive effects (why?)
- Thrombi of infected veins are called thrombophlebitis. They are the source of infected emboli (pyemia).

3- Thrombi of small or medium sized arteries (coronaries, cerebral) and almost all venous thrombi occlude the lumen and prevent blood flow.....Occlusive thrombi.

4- Thrombi over cusps of the heart are called vegetations.

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<tr>
<th>Site</th>
<th>Predisposition to thrombosis</th>
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<td>Artery</td>
<td>Atheroma</td>
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<td></td>
<td>Aneurysms</td>
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<tr>
<td>Heart valve</td>
<td>Inflammation caused by infection</td>
</tr>
<tr>
<td>Ventricle</td>
<td>Inflammation following infarction</td>
</tr>
<tr>
<td></td>
<td>Ventricular aneurysm</td>
</tr>
<tr>
<td>Atrium</td>
<td>Atrial fibrillation (→ stasis)</td>
</tr>
<tr>
<td></td>
<td>Mitral valve stenosis</td>
</tr>
<tr>
<td>Vein</td>
<td>Slow flow</td>
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<tr>
<td></td>
<td>Changes in coagulability of blood</td>
</tr>
<tr>
<td>Cerebral venous sinus</td>
<td>Inflammation following infection</td>
</tr>
<tr>
<td></td>
<td>Change in coagulability of blood</td>
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</table>

Coronary artery thrombosis on top of atheroma

- Conditions associated with an increased risk of thrombosis
1- Deep venous thrombosis of LL (DVT) less commonly superficial varicosities.

2- Massive tissue damage e.g. trauma, burns or major surgery are commonly associated with thrombosis. Increased blood coagulability and prolonged bed rest resulting in stasis are responsible factors.
3- Pregnancy and obstetric conditions, prolonged use of oral contraceptives, and steroid therapy.
4- Myocardial infarction, strokes and atherosclerosis.
5- Tumors...release thromboplastin....++ thrombosis.

* Outcome of thrombosis

1- Resolution:-
Fibrinolysis of the thrombus is mediated by plasmin. Since the endothelium lining veins produce more plasminogen activator, venous thrombi are resolved more readily than arterial and cardiac thrombi.

2- Propagation:-
Due to deposition of more platelets, fibrin and RBCs. A tail is formed which is more liable for detachment and embolization.
- Propagation occurs more with venous thrombi and progress towards the direction of the heart.

3- Embolization:-
- Due to detachment of thrombi from vessel wall. Septic thrombi produce pyemia.

4- Organization:-
Ingrowth of granulation tissue from vessel wall into the thrombus. Later on it changes to fibrous tissue which may be incorporated into the vessel wall.

5- Recanalization :-
Blood vessels in the granulation tissue may fuse into larger channels that bridge the thrombus with partial restoration of the blood flow in the affected vessel.
**Embolism**

- **Definition**
  It is a detached intravascular solid, liquid or gaseous material that is carried by blood to a site distant from its point of origin to be impacted in a small blood vessel.

- **Types**
  1. 99% thrombo-embolism
  2. Fat emboli
  3. Parasitic emboli
  4. Air or nitrogen emboli
  5. Amniotic fluid emboli
  6. Tumor emboli
  7. Cholesterol emboli...from atheromatous plaques.
  8. Fragments of bone marrow...after bone fracture.
  9. Foreign body emboli...cotton, talc powder, bullets

- **Clinically most important emboli are:-**
  1. Venous emboli....originating mostly from thrombi of the leg veins and produce pulmonary embolism.

  2. Arterial emboli....originating from the heart, aorta or large vessels and produce systemic embolism e.g. in the brain, kidney and spleen.

  3. Paradoxical embolism...originate as venous emboli, but instead of reaching the lungs they cross through a foramen oval or any right-to-left shunt in the heart to reach the arterial circulation.
**Pulmonary embolism**
- In 95% of cases they originate from thrombi of deep leg veins above the level of the knee.
- Effects on the lung depend upon the size of the embolus and state of the lung:
  1. 60-80% of cases are **small** and **clinically silent**.
  2. **Large emboli** that obstruct the pulmonary bifurcation (saddle emboli) or one of main pulmonary arteries.....**sudden death** (acute right sided failure) without manifestations of pulmonary infarction. **Why??**

- **Medium sized emboli**
  - with normal lung have no effect **why**?
  - With lung congestion it produce pulmonary infarction.
- **Small repeated emboli**
  With time they produce pulmonary hypertension ending in right -sided heart failure (cor-pulmonale)

**Systemic thrombo-embolism**
- These are emboli traveling in the arterial circulation.
- **Origin:**
  1. Intracardiac thrombi (over myocardial infarct, vegetations.
  2. Aorta and large vessels ( ulcerated atheromatous plaques or aortic aneurysm).
- **Sites of arrest**: usually multiple sites
  1. Lower extremities (75%) 2. Brain (10%)
  3. Intestine, kidney, spleen.
Effects:
Infarction of the affected organ

Septic thromboemboli...result from infected thrombi.
- Infarcts caused by these emboli become infected by bacteria and transform into abscess (pyemia)

Fat emboli

Causes:
- Fracture of long bones.
- Trauma or burn to fatty tissue.

Effects:
- Mechanical obstruction.
- Chemical release of FFA... local toxic effects with injury to vascular endothelium and platelet adhesion.

Air embolism

Causes:
1- Injury of jugular vein.
2- Childbirth or abortion.
3- Blood transfusion under positive pressure.

Effects:
- Small amounts...no effects
- More than 100 cc. ....Fill the right side of the heart.....acute heart failure....
Death.

What is decompression sickness (Caisson's disease)?
Infarction

*Definition:* An infarct is an area of ischemic necrosis caused by occlusion either of arterial blood supply or rarely the venous drainage of a particular tissue.

*Causes of vascular occlusion:*

A- Arterial occlusion.
- 99% of cases result from thrombo-embolism.
- Local vasospasm.
- Hemorrhage or ulceration in atheromatous plaque.
- External compression of the vessels E.g. by a tumor, edema, or strangulated hernia.
- Twisting of the vessels (testicular torsion or intestinal volvulus).
- Traumatic rupture of blood supply.

B- Venous occlusion
- Occurs mostly in organs with a single venous outflow e.g. testis or ovary.

*Types of infarction*

1- According to the color...pale and red
2- According to the presence or absence of infection...... Septic and bland (aseptic).
Testicular infarction
- It is red type of infarction. Caused mostly by torsion of the testis
- It is venous infarction

*Red infarction* Occurs in
1- Loose tissue (lung)...allows blood to collect easily.
2- tissue with dual blood supply (lung and intestine). blood escapes from the non occluded vessel.
3- Previously congested tissue.
4- Venous infarction.
5- When blood is re-established to a site of arterial occlusion and necrosis.

Cerebral boundary zone infarction
- It is due to systemic hypo perfusion.
- Occurs in areas of the brain supplied by small blood vessels at the borders farthest from the main arterial supply. It is always red infarction
**Pale infarction**  Occurs in
- Arterial occlusion in solid organs with end arterial occlusion (heart, kidney and spleen).

**Septic infarction**
- Caused by septic emboli, (vegetations from acute bacterial endocarditis)
- Produce multiple abscesses (pyemic abscesses).
- Usually fatal.

![Pale infarction kidney]

**Morphology of infarction**

*Grossly:* -
- Most infarcts are wedge-shaped with the occluded vessel at the apex and the periphery of the organ at the base.
- Serosal surface shows fibrinous exudates.
- Color may be red or pale.
- Margins are defined by a narrow rim of hyperemia and inflammation. (1-2 days later)
- Early infarcts are swollen ,late healed infarcts are retracted.

*Microscopically* -
- It is coagulative necrosis except in the brain ,it is liquifactive. A narrow zone of inflammation and congestion surrounds the infarct area.

![Kidney- coagulative](image1)
![Brain- liquifactive](image2)
![Narrow zone on inflam. & congestion](image3)
Clinical correlations:

- **Factors that affect the development of infarction**
  1. **Nature of the vascular supply.**
     Organs with double blood supply (lungs and liver) can better withstand infarction than organs with single blood supply (heart).
  2. **Rate of blood occlusion**
     Chronic, gradual occlusion has a better outcome as it gives a chance of collateral circulation to develop and save the organ.
  3. **Susceptibility of tissue to hypoxia**
     - Neurones (3-4 min) and myocardium (20-30 min) are highly sensitive to hypoxia.
     - Connective tissue (fibroblasts and skeletal muscles) are highly resistant.
  4. **Oxygen content of blood**
     Tissues having low oxygen partial pressure (congested, anemic, cyanotic) are more susceptible to infarction than normal well oxygenated tissues.

**Fate of infarction**

- Myocardial infarct... is replaced by a fibrous scar.
- Cerebral infarct....is liquefied, reabsorbed with resulting pseudocyst filled with fluid.
- Liver infarct....if small and framework is preserved.... Regenerate
  If large with destroyed framework .......Fibrosis.

Myocardial infarction

Brain infarct, Liquefaction and pseudocyst
Gangrene

- It is necrosis with superadded putrefaction caused by bacterial activity (of clostridia group) with the production of gases and toxins.
- It may be primary or secondary gangrene.

Primary gangrene

- A serious complication of deep war wounds contaminated by anaerobic gram positive bacilli of clostridia group.
- Anaerobic conditions + necrotic tissue + bacteria......tissue digestion with liberation of foul smelling gases.
- Condition is associated with severe toxemia and is rapidly fatal.

Dry gangrene:

- Occurs especially in toes and feet of elderly patients suffering from gradual arterial occlusion.
- There are minimal amounts of fluids due to patent venous and lymphatic drainage and evaporation from the surface.
- The putrefactive process is slow with a line of demarcation (area of inflammation) between the gangrenous and the healthy parts.

Wet (moist) gangrene :

- Tissues are moist at the start either from edema or venous congestion.
- Affects internal organs especially intestine (strangulated hernia, volvulus or intussusception) or leg vessels in diabetic patients or in crush injuries.
- Occlusion of both arterial and venous blood vessels.
- There is no line of demarcation.
The putrefactive process is rapid and associated with severe toxemia.

Moist gangrene (intestine)  Intussusception

**Shock**

- **Definition:**
  It is systemic hypoperfusion due to a reduction either in cardiac output or in the effective blood volume.

- **Causes:** Three main causes and other less common causes.
  1. **Cardiogenic shock** — due to pump failure resulting from
     a. Extensive myocardial infarction, ventricular arrhythmias, or cardiac tamponade
     b. Outflow obstruction due to massive pulmonary embolism.
  2. **Hypovolemic shock** — due to hemorrhage or plasma loss as in burns, trauma.
  3. **Septic shock** — due to systemic microbial infection mostly by gram negative bacteria (endotoxic shock).

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<th>Clinical Examples</th>
<th>Principal Mechanisms</th>
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<td>Cardiogenic</td>
<td>Myocardial infarction, ventricular rupture, arrhythmia, cardiac</td>
<td>Failure of myocardial pump due to intrinsic myocardial damage or extrinsic pressure or obstruction to outflow</td>
</tr>
<tr>
<td></td>
<td>tamponade, pulmonary embolism</td>
<td></td>
</tr>
<tr>
<td>Hypovolemic</td>
<td>Hemorrhage, fluid loss, e.g., vomiting, diarrhea, burns, trauma</td>
<td>Inadequate blood or plasma volume</td>
</tr>
<tr>
<td>Septic</td>
<td>Overwhelming microbial infections, endotoxic shock, gram-positive septicemia, or fungal sepsis</td>
<td>Peripheral vasodilation and pooling of blood; endothelial activation/injury; leukocyte-induced damage; disseminated intravascular coagulation</td>
</tr>
</tbody>
</table>

- **Less common causes**
  5. Anaphylactic shock — IgE mediated — release of histamine — peripheral vasodilatation and increased vascular permeability.

**Pathogenesis of septic shock:**
Due to bacterial wall lipopolysaccharides (LPSs).

A- **At low doses**, (LPSs) activate monocytes, macrophages and neutrophils to eliminate the bacteria. Activated mononuclear cells secrete cytokines (TNF, IL-1, IL-6 AND IL-8).

B- With **moderate doses** of (LPSs), more cytokines are produced with systemic manifestations - TNF and IL-1.....Fever and leucocytosis.

- Secondary effectors (NO, PAF) are produced.

C- With still **higher doses**, high levels of cytokines and secondary effectors produce - Systemic VD.......(hypotension).

- Diminished myocardial contractility.

- Widespread endothelial injury....leucocyte adhesion and diffuse alveolar capillary damage in the lung (Adult Respiratory Dystress Syndrome).

- Activation of coagulation system.....DIC.

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**Pathogenesis of septic shock**

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Stages of shock

- Three stages one leads to the other if the underlying cause is not corrected.
  1. Non progressive stage.
  2. Progressive stage.
  3. Irreversible stage

1- Non progressive stage

- The body tries to restore its normal cardiac output and blood pressure by
  - ++ Baroreceptor reflexes......Tachycardia.
  - Release of catecholamines + sympathetic stimulation......Peripheral VC....skin pallor.
  - ++ Of rennin-angiotensin-aldosterone axis + secretion of ADH....Renal conservation of fluid.
  - Coronary and cerebral vessels are less responsive to sympathetic stimuli therefore they maintain their normal caliber, blood flow and oxygen delivery to their organs.

2- Progressive stage ......Is characterized by

- Hypotension and decreased cardiac output.
- Tachypnea and dyspnea later on pulmonary edema develops which further worsen pulmonary functions.
- Oliguria (urine output <500 cc/day) due to renal VC and reduced glomerular filtration rate. - Acidosis ...both metabolic and respiratory.

3- Irreversible stage

- Complete circulatory collapse and marked hypoperfusion of vital organs leading to DIC, loss of vital functions and multiple organ failure which cannot be corrected and progress to death
- Marked hypotension and extreme tachycardia.
  - Respiratory distress not responding to O2 therapy or ventilator.
  - Loss of consciousness ending in coma. - GIT bleeding.
  - Anuria with elevation of BUN and serum creatinin.
- Severe acidosis.  
- Laboratory signs of DIC

- Lungs...Adult respiratory distress syndrome (ARDS).
- Gastrointestinal tract...mucosal ischemia,...multiple hemorrhages, ulcerations and necrosis.
- Kidney...Acute tubular necrosis.
- Liver...Centrilobular necrosis.
- Brain...Ischemia, focal hemorrhage and necrosis.
- Adrenals...Hemorrhages and cortical necrosis.

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Early shock</th>
<th>Late shock</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>Pale and cold</td>
<td>Cyanosed</td>
</tr>
<tr>
<td>Kidneys</td>
<td>Low urine production</td>
<td>Necrosis of tubular epithelium</td>
</tr>
<tr>
<td>Gut</td>
<td>Bowel stasis</td>
<td>Necrosis of lining epithelium</td>
</tr>
<tr>
<td>Lung</td>
<td>Tachypnoea</td>
<td>Necrosis of alveolar epithelium</td>
</tr>
<tr>
<td>Liver</td>
<td>Fatty change</td>
<td>Necrosis of centrilobular cells</td>
</tr>
<tr>
<td>Brain</td>
<td>Reduced conscious level</td>
<td>Necrosis of neurons, coma</td>
</tr>
<tr>
<td>Heart</td>
<td>Tachycardia</td>
<td>Myocardial necrosis</td>
</tr>
</tbody>
</table>

Fig. 8.8 Early and late manifestations of shock.

Morphology of organs affected by shock