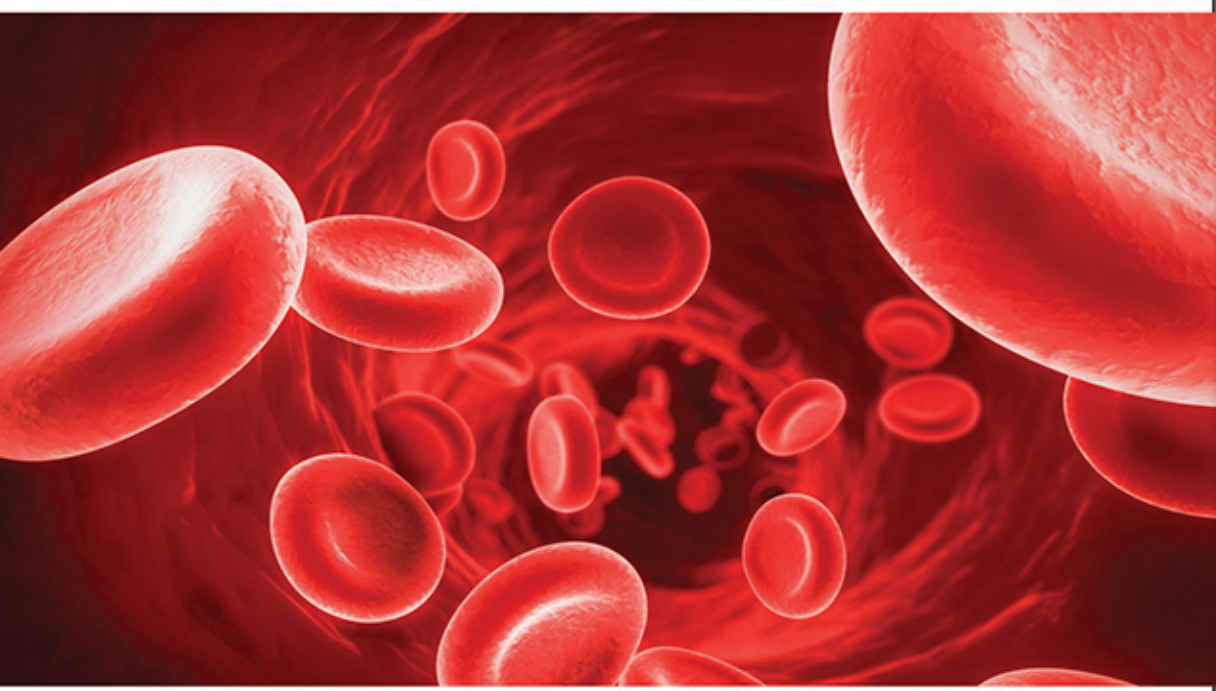
A Short Textbook of PATHOLOGY

(General Pathology, Systemic Pathology, Hematology, Clinical Pathology, and Molecular Techniques in Laboratory with Practical notes and Important SAQs/MCQs)

SECOND EDITION



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Foreword
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Chapter 7

Hemodynamic Derangement

Normal functions of cells, tissues and organs depends on uninterrupted circulation which delivers oxygen and nutrients and remove carbon dioxide to and from these structures. This is called normal fluid homeostasis and this depends on maintenance of vascular wall integrity and intravascular pressure and osmolarity in physiologic ranges. Normal fluid homeostasis also maintains blood in a liquid state. So any alteration of normal fluid homeostasis will give rise to water movement from vessel to extravascular space known as edema which when accumulates in lung in excess amount can cause difficulty in breathing called breathlessness, swelling of affected parts causes ***edema*** of legs. Also sometimes an injury to blood vessels can cause extravasation of blood and accumulation of excess of blood in tissue, organ known as ***hematoma*** or may lead to clotting of blood in an injured tissue, organ known as ***thrombosis***, clot migration to other places known as ***emboli*** and cell or tissue death called ***infarction***.

NORMAL HOMEOSTASIS

At the site of a vascular injury there is brief period of arteriolar vasoconstriction that follows neuroorganic mechanism and is augmented by local secretion of factors like endothelin, an endothelium derived vasoconstrictor but this is transient response. Endothelial injury exposed the most potent thrombogenic substance the subendothelial collagen which allows platelet to adhere and get activated. Due to platelet activation there is marked shape change in platelets and release of secretory granules. Secreted products recruits more platelets and forms a homeostatic plug known as ***primary homeostasis***. Tissue factor released at the site also known as factor III and thromboplastin is a membrane bound procoagulant glycoprotein synthesized by endothelium. It acts with factor VII and activate coagulation cascade ultimately leading to thrombin generation. Thrombin cleaves circulatory fibrinogen to insoluble fibrincreating a fibrin meshwork deposition. Thrombin also cause further platelet recruitment and granule release known as ***secondary homeostasis.*** Finally polymerization of fibrin and platelet aggregation forms a solid permanent plug to prevent any additional hemorrhage. At this stage tPA is set into motion to limit homeostatic plug at the site of injury, now we can turn into derangements of this normal homeostasis.

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THROMBUS

Definition

Formation of a solid or semisolid mass in the living circulation from the constituents of blood is called a thrombus.

Etiology

Explained by Virchow's triad which includes:

1. ***Endothelial injury:*** Important in thrombus formation in heart/arterial circulation. Intact endothelium does not allow platelet and plasma coagulation factor to come in contact with the most potent thrombogenic agent the subendothelial ECM. Platelets must also be activated to adhere to injured site. Nonactivated platelet cannot aggregate. Activated platelets are also prevented from aggregation by PGI_2 and NO, both are potent vasodilator and inhibitor of platelet aggregation. Activated platelet expresses procoagulant proteins like tissue factor, vWF that leads to thrombus formation. Endothelial injury may be induced by two ways:
   a. *Direct endothelial injury:* Endocardial injury due to myocardial infarction, ulcerated plaques in atherosclerotic arteries and traumatic or vascular injury (vasculitis). Here the direct endothelial injury causes exposure of subendothelial ECM which is the most potent platelet aggregator, then there is adhesion of platelets, release of tissue factors, local depletion of PGI_2 and PAs leading to thrombus formation.
   b. *Endothelial dysfunction:* Hemodynamic stress due to hypertension, turbulent flow over damaged valves, or bacterial endotoxin.
   c. *Procoagulant factors:* Platelet adhesion molecules, tissue factor, PAI. Once there is endothelial injury there is exposure of subendothelial ECM that cause platelet aggregation. After endothelial injury the endothelial cells express vWF and tissue factor that allows rapid binding of basement membrane and aggregation of platelets through glycoprotein Ib receptor. Release of cytokines TNF, IL1, bacterial endotoxin activate extrinsic pathway by activating IXa, Xa. Endothelial cells also secrete PAI that depresses fibrinolysis.
   d. *Anticoagulant and antithrombic factor:* Thrombomodulin, PGI2, t-PA, NO, intact endothelium. PGI2 and NO potent vasodilator and platelet aggregate inhibitor. Intact endothelium prevents platelet aggregation by covering the potent subendothelial ECM.Endothelial cells synthesize tPA promoting fibrinolytic activity to clear fibrin deposition from endothelial cell surface.

   If dynamic imbalance between anti-and procoagulation factors persists and if the procoagulation factors get upperhand then there is thrombus formation.
2. ***Alteration of blood flow:*** Leading to countercurrent and stasis. Countercurrent leads to the formation of obstruction to blood flow and stasis leading to the accumulation of prothrombotic factors. Stasis results in slow clearing of anticoagulation factors. These result in thrombus formation. This is particularly important in development of thrombus in venous circulation particularly in deep vein of leg.
3. ***Hypercoagulability:*** Less frequent contributor, alteration of coagulation pathway that predisposes to thrombosis. There are two main causes of hypercoagulability.
   a. *Primary (hereditary) causes:* Genetic mutation of prothrombin gene, Factor V gene.

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b. *Secondary (acquired) causes:* More common causes include: Immobilization, bedridden for long time, obstetric causes
Less common cause includes: Smoking.
c. High risk for thrombosis—Prolonged bed rest or immobilization, MI, atrial fibrillation, tissue damage (surgery, fracture or burn), Cancer, DIC, prosthetic cardiac valves. Low risk for thrombosis—cardiomyopathy, hyperestrogenic states (pregnancy), oral contra-ceptive, sickle cell anemia, smoking.

Differences between Arterial and Venous Thrombi

Usually occlusive	Invariably occlusive
Moves away from heart	Moves towards heart
Color: Pale platelet/fibrin deposition	Red due to enmeshed RBCs
Common sites: Cardiac, cerebral, femoral	Popliteal, femoral, Iliac, other plexuses

Differences between Thrombus and Postmortem Clot

Formed in living circulation	Nonliving circulation, e.g. test tube, dead body
Attached to underlying vessel wall	Not attached to underlying vessel wall
Not easy to remove	Can be peeled off easily
Lines of Zahn	Gelatinous coagulum of blood
Alternate deep/pale color	RBCs settle down, supernatant yellow chicken fat appearance
Alternate layer of platelets and fibrin	WBC, RBC, platelet

FATE OF A THROMBUS

a. ***Propagation:*** Accumulates more platelet and fibrin, eventually leading to vessel occlusion
b. ***Embolization:*** Thrombi may dislodge and travel to other sites of vasculature
c. ***Dissolution:*** Thrombi may be removed by fibrinolytic activity
d. ***Organization and recanalization:*** Thrombi may induce inflammation and fibrosis and may eventually become recanalized—reestablishing blood flow—may be incorporated into a thickened vascular wall.

TYPES OF THROMBUS

Thrombus is classified depending on:
a. ***Origin,*** e.g. arterial or venous thrombi
b. ***Color:*** Red or pale thrombi
c. ***Nature of occlusion:*** Occlusive/nonocclusive
d. ***Lodgement of thrombi:*** In cardiac chambers—***mural thrombi*** damaged valve-***vegetation***, may be ***sterile (noninfected)***, or ***septic (infected)***, infected endocarditis due to bacterial or fungal infection)), ***verrucous (Libman-Sacks)*** endocarditis due to circulating immune complex.

Clinical Importance of Thrombosis

The importance of thrombi lies in the fact that they are ***the major source of embolism*** and they can cause ***arterial or venous obstruction***. The clinical feature depends on

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onset, occlusion, associated infection and the status of the vessel and availability of collateral circulation. When arterial thrombi lodges in critical sites like coronary artery they cause myocardial infarction, if cerebral arteries are occluded then stroke, para and hemiplegia, intracranial hemorrhage. Thrombi can also lodge in kidney, spleen and cause infarction, hemorrhage. ***Causes of arterial thrombi includes atherosclerosis, endothelial injury, endothelial dysfunction, damaged valves.***

Venous Thrombi

Venous thrombi can be lodged in both superficial and deep vein causing congestion and edema in vascular bed distal to occlusion. In superficial venous system, i.e. saphenous vein due to varicosity it causes swelling, local congestion, pain, tenderness along the course of the vein. Overlying skin is traumatized frequently and cause varicose ulcers. Deep vein thromboses are serious because they embolize. 50 percent cases deep vein thrombosis is clinically silent and clinical symptoms only appear when it embolizes.

Causes of Venous Thrombosis

1. Stasis and hypercoagulable states as in late pregnancy, postpartum period and during delivery amniotic fluid embolism
2. Cardiac failure
3. Trauma, surgery, burn
4. Reduced physical activity, immobilization, injury to blood vessels
5. Tumor associated procoagulation factor release so called migratory thrombophlebitis or Trousseau sign.

EMBOLUS

An embolus is a detached solid, liquid, gaseous mass that is carried by the blood to a site distant from its point of origin.

Source

Ninety-nine percent arise from thrombus, as such the term ***thromboembolism*** applies. Rare causes includes gaseous, air, amniotic fluid, foreign body, parasite, fat, etc.

TYPES

Pulmonary Thromboembolism

They usually originate in deep vein of leg, travels via large venous channels, passes through right side of heart and enter the pulmonary vasculature. Depending on the size and number it may cause:

Most pulmonary emboli are clinically silent because of their small size. Majority are incorporated or organized. If 60-80 percent pulmonary circulation is compromised then there may be sudden death due to right heart failure or cor pulmonale. If large and occlude main pulmonary bifurcation-saddle emboli, may shower the pulmonary vascular bed, may pass through interventricular or interarterial septa and ***go to systemic circulation-paradoxical emboli***. Most pulmonary emboli are clinically silent because of their small size. Majority are incorporated or organized.

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If 60-80 percent pulmonary circulation is compromised then there may be sudden death due to right heart failure or cor pulmonale. ***Emboli of medium size may cause hemorrhage*** but do not cause infarction as there is dual blood supply. If there is preexisting left sided cardiac failure may result in infarct. ***Embolic obstruction in small end pulmonary arteries can cause infarction***. Multiple emboli over passage of time may develop ***pulmonary hypertension and right heart failure.***

Systemic Thromboembolism

Majority of systemic emboli develop from ***wall of heart (mural thrombi)*** and associated with left ventricular wall infarct or atrial fibrillation. Some can occur from ***aortic aneurysm, ulcerated atheromatous plaques, fragmentation from vegetations***. The major sites of arterial emboli are lower extremities (75%), brain (10%) and remainder in intestine, kidney, spleen and upper extremities. The effect of arterial emboli depends on extent of collateral supply, vulnerability of tissue to ischemia and the caliber of the vessels occluded. When emboli travels arterial circulation it is called **systemic emboli**.

Fat Embolism

After fracture of long bones and soft tissue trauma or burns there may be accumulation of fat and then it may enter the circulation via marrow vascular sinusoids. Minimum 100 cc/ml of fat is required to develop fat embolism. Fat embolism syndrome is a rare entity characterized by cardiopulmonary symptoms like dyspnea, tachycardia, tachypnea after 1-3 days of injury. May be associated with anemia and thrombocytopenia. The pathogenesis is probably due to mechanical obstruction by fat emboli and biochemical injury. Microemboli may cause activation of platelets, RBCs, granulocyte recruitment with release of free radicals, release of fatty acid from fat globules causing local toxic injury to endothelium.

Air/Gas Embolism

Gas/air bubbles may aggregate and cause vascular flow obstruction causing ischemic injury. Air may gain access by obstetric procedures, IV injections/drips or traumatic chest wall injury. At least 100 cc/ml is required to form an emboli. The bubbles act like a physical agent and obstruct the flow. A special type of gas embolism is called decompression sickness. When an individual is exposed to sudden atmospheric change from high pressure to low pressure quickly, gas bubbles particularly nitrogen gas dissolved in blood and tissues and forms emboli. It occurs in people in unpressurized aircraft, scuba or deep sea divers, underwater construction workers. It is of two types acute and chronic. In acute cases gas bubbles are formed in skeletal muscles, joints and its supporting tissues it causes painful condition called bends. Gas emboli can also cause focal ischemia in a number tissues including brain, heart, lung and may develop edema, hemorrhage and atelectasis, emphysema leading to dyspnea called chokes. A chronic form is known as Caisson disease. Here gas embolism in skeletal system causes multiple foci of ischemic necrosis common sites are heads of femur, tibia and humerus.

Amniotic Fluid Embolism

It is a very grave and uncommon complication of pregnancy in labor and postpartum period with a high mortality of 20-40 percent as with other important complications

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like eclampsia and pulmonary embolism. During parturition via placental tear fetal elements like fetal squames, lanugo hair, fat from vernix caseosa and mucin from fetal respiratory or gastrointestinal tract enter maternal circulation and cause DIC. The onset is sudden, rapid with severe dyspnea, cyanosis, hypotension and shock followed by convulsion and coma.

Parasitic Embolism

Caused by impaction of *Scistosomiasis* and *Trichinella spiralis* in circulation.

Foreign body embolism caused by bullets, pillets of guns.

Hyperemia

Indicate a local increase in blood volume to a particular tissue. Hyperemia is an active process, congestion is a passive process. In hyperemia there is increased blood flow due to arteriolar dilatation. So it is seen at the site of inflammation and in skeletal muscle during exercise. In hyperemia there is also engorgement due to increased blood flow with oxygenated blood.Conversely in congestion there is increased deoxygenated hemoglobin containing blood so the affected part is pale, bluish cyanotic in color.

Hemorrhage: Extravasation of blood due to vessel rupture.

Bruise: Minute insignificant hemorrhage is called bruise. It is common in older reproductive women particularly in buttocks.

Petechia: Small minute hemorrhage 1-2 mm in diameter, pin head in skin, mucosa, serosal surface. It occurs due to local increased vascular pressure, Reduced count and defect in platelet function, clotting factor deficiency.

Purpura: Hemorrhage in skin, mucous membrane, organ >3 mm in diameter. Commonly associated with causes of petechia and also found after trauma, vasculitis and increased vascular fragility.

Ecchymosis: Subcutaneous hemorrhage >1-2 cm usually following trauma but can also occur in conditions mentioned in petechia and purpura. There are color changes in hematoma. First, it is red blue in color due to degradation and phagocytosis of RBCs by macrophages and liberation of hemoglobin. Then after conversion to bilirubin gives blue green color. Finally converted to hemosiderin giving a golden brown color.

Larger accumulations of blood within tissue is called **hematoma**. If ***hematoma*** occurs in brain, retroperitoneum then the clinical effect is grave and if untreated it may be fatal.

Accumulation of Blood in Body Space or Cavities

- ***Pleural cavity:*** Hemothorax
- ***Peritoneal cavity:*** Hemoperitoneum
- ***Pericardium:*** Hemopericardium
- ***Joint space:*** Hemoarthritis.

CONGESTION

It is a passive process which occurs due to impairment of venous drainage. It also indicate local increase in blood volume to a particular tissue. It may be localized (due to venous obstruction) or systemic (in cardiac failure). The affected tissue becomes cyanosed (blue-red color) due to accumulation of deoxygenated hemoglobin. Liver, lung, spleen are mostly affected tissue.

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Morphology

The cut surface of both hyperemic and congested tissue is hemorrhagic and wet. Chronic congestion of liver leads to **nutmeg appearance liver** characterized by the presence of central brown region due to loss of hepatocytes and peripheral surrounding zone of uncongested tan hepatic cells. In long-standing cases of heart failure hepatic fibrosis is evident known as cardiac cirrhosis.

Microscopic Examination of Acute Congestion

Lung: Alveolar capillaries are full of blood and alveolar septa show edema and focal intraalveolar hemorrhage.

Liver: Central vein and sinusoids are distended with blood. Central hepatocytes may show degeneration, while peripheral hepatocytes show only fatty change because of adequate blood supply.

Microscopic Examination of Chronic Congestion

Lung: The alveolar septa is thickened and fibrosed and there is accumulation of heart failure cells in the alveoli (hemosiderin laden macrophages are called **heart failure cells**).

Liver: Microscopically there is centrilobular necrosis with loss of hepatocytes, areas of hemorrhage and presence of hemosiderin laden macrophages.

Infarct: An infarct is an area of ischemic necrosis caused by occlusion of either the arterial supply or the venous drainage in a particular tissue. The process of formation of a infarct is known as infarction.

Almost 99 percent of all infarcts result from thrombotic or embolic events and almost all result from arterial occlusion.

Types

White (solid tissue with end arteries like heart, kidney, spleen and arterial occlusion) and ***red*** infarct (spongy tissue like lung, dual circulation like liver, lung, forearm, single artery with large anastomosis like intestine, occlusion or torsion of venous return ovary, testis, intestine) (Table 7.1).

Clinical features depends on:

a. ***Nature of vascular supply:*** Infarct takes time to develop in dual circulated areas like lungs (pulmonary vein and arterial system), liver (hepatic and portal system), forearm (ulnar and radial circulation).

Table 7.1 Differences between white and red infarct

Features—white infarct	Red infarct
Occurs usually in solid organ	Occurs in loose tissue and sometimes in solid organ, ovary and testis after torsion
Status of circulation occurs in arterial occlusion (with end arteries)	Occurs in venous occlusion or tissue with dual circulation
Example: Heart, kidney, spleen	Example: Lung, small intestine, brain

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b. ***Rate of development of occlusion:*** Slowly developing infarct has less impact than rapidly developing infarct.
c. ***Vulnerability to hypoxia:*** Permanent tissues like neural and cardiac muscle develop infarction more rapidly than mesenchymal tissue-like fibroblasts.
d. ***Oxygen content of blood:*** Infarction develops more rapidly in anemic, cyanosed and atherosclerotic patients who has compromised blood flow than people having normal circulation and oxygen content.

Morphology of an Infarct

Most infarcts are wedge-shaped with occluded vessel forming apex and periphery of the organ forming the base. The margins are irregular and poorly defined initially but with time it becomes well-defined by a narrow rim of hyperemia. In white infarct the extravasated RBC are lysed and produce hemosiderin which are not so significant. They become progressively pale and sharply defined with time. But in case of red infarct the hemorrhage is extensive and produce hemosiderin in profuse amount so it become more firm and brown in course of time.

Histologically

The predominant feature in an infarction is coagulative necrosis except the brain where liquefactive necrosis occurs. An inflammatory response occurs in the margins within hours to days and the tissue debris are removed by macrophage and neutrophils. Then ultimately the infarcts are replaced by scar tissue. Septic infarction may occur in heart valves where embolization occurs due to bacterial vegetation or sometimes abscess may develop in the infarcted area.

CLINICAL EFFECTS OF INFARCTION

1. Myocardial infarction in case of coronary heart disease
2. Cerebral infarction
3. Pulmonary infarction
4. Peripheral vascular disease.

Myocardial Infarction

Definition: Myocardial infarction is the most important form of ischemic heart disease occurs due to either sudden or gradual occlusion of one or more coronary arteries.

Common site of infarction: The narrowing of main arterial trunks and associated myocardial infarction is as follows:
a. ***Left anterior descending coronary arteries (40-50%):*** Infarction involves anterior wall of left ventricle near apex, anterior two-third of interventricular septum.
b. ***Right coronary artery (30-40%):*** Infarction involves posterior wall of left ventricle and posterior one-third of interventricular septum.
c. ***Left circumflex coronary artery (15-20%):*** Lateral wall of left ventricle.

Types

There are two main types of myocardial infarction:

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a. ***Transmural infarction:*** When the ischemic necrosis involves the full thickness of the ventricular wall and is at least 2.5 cm in diameter.
b. ***Subendocardial (nontransmural):*** When areas of ischemic necrosis is limited to inner one-third or at most one-half of the ventricular wall.

Virtually all transmural infarct involve the left ventricle including interventricular septum. Isolated infarction of the right ventricle occurs in one-third of cases.

Causes

Age: MI can occur at any age but the peak range is between 40-65 years.

Sex: Males are at higher risk than females but female preponderance is seen in diabetic female especially postmenopausal due to lack of estrogen which imparts a protective factor in reproductive menstruating female.

Exogenous factors: Like smoking, oral contraceptive use, physical inactivity, sedentary lifestyle, alcohol, obesity, dyslipidemia influences the disease.

Coronary artery occlusion: Ninety percent of transmural infarct is caused by an occlusive intracoronary thrombus overlying as ulcerated or fissured stenotic atheroma. Platelet aggregation and activation and vasospasm contribute to the acute event.

Other factors: That increases myocardial demand are: Tachycardia, hemodynamic events as hypotension, hypercholesterolemia worsens the condition.

Morphology

Gross/naked eye: No change detectable in 6-12 hours.
A slight pallor may be seen after 18-24 hours.
Paler, red blue cyanotic myocardium 3-7 days.

1st week: Sharply defined, yellow, well-demarcated, some softened area rimmed by a hyperemic moist narrow zone of highly vascularized central zone.

Microscopical Findings

a. ***4-8 hours:*** Necrosis is not detectable, stretching and waviness of myocardial fibers within infarct.
b. ***12 hours:*** Beginning of coagulation necrosis, edema, hemorrhage, neutrophilic infiltration.
c. ***18-24 hours:*** Coagulative necrosis marked, infiltration of neutrophil in the interstitium.
d. ***3-7 days:*** Marginal fibrovascular response, dead resorption of sarcoplasm.
e. ***10 days:*** Well-developed necrotic changes. Presence of fibrovascular reaction in the margin.

Tests Done for Diagnosis

ECG changes: New Q wave.
ST segment elevation.
T wave change inversion.
Arrhythmias.

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Echocardiography:
- Color Doppler
- ETT
- Angiogram (CAG, CT angiogram)
- Radioisotope scanning
- MRI.

CARDIAC ENZYMES

Most of these cardiac emzymes are cytoplasmic enzymes and leak out from lethally damages myocardial cells. Of these the early and most specific marker is Troponin I and T. Troponin is required for myocardial contraction. So any injury to myocardium will lead to its leakage and this is tested in the laboratory. Any healthy people if tested routinely and there is elevated Troponin I and T, should be treated even in absence of symptoms of MI. Similarly creatinine phosphokinase particularly M Band (CK-MB) is also specific for MI.

Early markers: Troponin I and T, CK-MB-rises above baseline within 4-8 hours, reaches peak very early and falling to baseline within 4 days. The troponins are also released in unstable angina with minimal cardiac damage (normal upto 1 ngm/ml).

Intermediate markers: SGOT-begins to rise in 8 hours, reaches peak at 18-36 hours and return to baseline in 4 days (normal upto 35 IU/l).

Late markers: LDH- begins to rise at 24 hours, reaches peak in 3-6 days and returns to base at the end of second week (normal 230-460 IU/l).

Clinical Features

Sudden constrictive crushing bearing substernal or precordial pain often radiating to left shoulder, arm, jaw, sweating, nausea, vomiting, breathlessness, indigestion or heart burn. Fifteen percent cases present as asymptomatic.

Complications (Outcome of MI)

a. Uncomplicated cases—10-20 percent
b. Complicated cases—Cardiac arrhythmia in 75-95 percent of cases,
   - Left ventricular congestive failure with
   - Pulmonary edema (60%)
   - Thromboembolism (15-40%)
   - Cardiogenic shock (10%)
   - Rupture of wall, septum, papillary muscle (1-5%).

EDEMA

Abnormal collection of fluid in the interstitial tissue space or body cavities is called edema. Edema can also be defined as extravasation of fluid from vessels to interstitial spaces. The fluid may be protein poor ***(transudate)*** or protein rich ***(exudate)***.

Types of Edema

1. ***Depending on accumulation of edema fluid***
   a. Generalized edema is also known as ***anasarca***.
   b. Local edema—Confined to one organ, tissue, parts

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c. Pitting edema—Subcutaneous edema which cause pitting and displacement of edema fluid on finger pressure and again comes back when the pressure is withdrawn
d. Accumulation in body cavities.

Edema fluid accumulation in pleural cavity—**Hydrothorax**
Edema fluid accumulation in pericardial cavity—**Hydropericardium**
Edema fluid accumulation in peritoneum—**Hydroperitoneum** or **ascites**
Edema fluid accumulation in joint cavity—**Hydroarthrosis.**

2. ***Depending on the pathophysiology:***
   a. *Increased hydrostatic pressure:* Causes are congestive cardiac failure, constrictive pericarditis, ascites due to liver cirrhosis, thrombosis, arteriolar dilatation due to heat and neurohumoral excess. These conditions lead to decreased cardiac output and decreased renal perfusion which triggers the rennin-angiotensin aldosterone system. As a result there is sodium and water retention and edema.
   b. *Decreased plasma oncotic pressure:* It causes include nephrotic syndrome, liver cirrhosis, malnutrition and protein losing enteropathy. Here reduced albumin synthesis leads to reduced plasma oncotic pressure as a result there is movement of fluid to tissue space plus there is plasma volume contraction. These leads to reduced intravascular volume, reduced hypoperfusion, secondary aldosteronism and edema.
   c. *Lymphatic obstruction:* Which may be due to inflammation, neoplasia, postsurgical and postradiation. Filariasis cause massive lymphatic and lymph node fibrosis leading to impaired lymphatic drainage and local edema specially in inguinal region, genitalia and lower limbs. In breast cancer obstruction of superficial lymh nodes leads to edema of overlying skin known as peau d orange (orange peel) and after radical mastectomy there is surgical removal of axillary lymph nodes which leads to severe edema of arm in breast cancer patient.
   d. *Sodium retention:* Due to excessive salt intake, increased tubular re absorption of sodium, renal hypoperfusion and increased rennin-angiotensin-aldosterone secretion.
   e. *Inflammation:* Including acute and chronic inflammation and angiogenesis. There is increased vascular permeability and outpouring of protein-rich fluid (exudation) leading to edema.

Morphology of Edema

Naked eye/grossly edema is easily recognizable by swelling of the affected parts.

For example, in generalized brain edema the brain is grossly swollen with narrowed sulci and distended gyri.

Brain edema may be local due to abscess or neoplasm and may be generalized, causes include encephalitis, hypertensive crisis, obstruction to brain venous outflow.

Subcutaneous edema may diffuse or may be seen at the site of highest gravitation like dependent parts and sacrum.

Edema of dependent part is a feature of right ventricular failure.

Renal edema may be generalized or may manifest in loose and lax tissues and as such it is more manifested under lower eyelids.

Periorbital edema is characteristic of severe renal disease.

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Pitting edema is manifested by displacement of edema fluid by finger pressure leaving behind a pit or finger shaped depression and again coming back after withdrawal of finger pressure.

Pulmonary edema is seen in left-sided ventricular failure.

Microscopically edema is manifested by subtle cell swelling, clearing and separation of extracellular matrix.

Clinical Importance of Edema

a. ***Signals underlying disease:***
   - ❖ Example—Subcutaneous tissue edema is indicative of cardiac or renal failure
   - ❖ Edema of lower eyelid is indicative of renal disease
   - ❖ Elephantiasis is indicative of filariasis
   - ❖ Swelling of forearm after radical mastectomy is indicative of lymphatic edema.

b. ***Impairs wound healing and clearance of infection:*** Because edema fluid cause vascular ischemia and excellent environment for microbial multiplication.

Outcome of Edema

Depends on organ involvement, for example:

a. ***Brain edema:*** Serious and may be fatal. Herniation of brain substance through foramen magnum or compression of vascular supply is fatal because both can cause injury to medullary center.

b. ***Pulmonary edema:*** It can cause death by interfering with normal ventilatory function due to accumulation of fluid in alveoli cause ischemia of vessels in alveolar septa and edema fluid is a very good soil for microbial multiplication leading to septicemia and bacteremia.

Definition

Shock or cardiovascular collapse, is the final common pathway for a number of lethal clinical events, including severe hemorrhage, extensive trauma or burns, large myocardial infarction, massive pulmonary embolism and microbial sepsis. The main effect of shock is systemic hypoperfusion due to either reduced cardiac output or ineffective circulating blood volume ultimately causing hypotension followed by impaired tissue perfusion and cellular hypoxia.

Types

Cardiac shock results from myocardial pump failure. This may be caused by intrinsic myocardial damage (infarction), ventricular arrhythmia, extrinsic compression (cardiac tamponade), or outflow obstruction (pulmonary embolism).

Hypovolemic shock results from loss of blood or plasma volume. This may be caused by hemorrhage, fluid loss from severe burn, or trauma, severe diarrhea, vomiting, sweating.

Septic shock is caused by systemic microbial infection most commonly by gram-negative organisms (endotoxic shock) and less commonly by gram- positive organisms exotoxin producing.

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This book was published by the authors at their own effort, cost and sincerity in 2009 in Dhaka, Bangladesh with a clear aim to understand the subject Pathology in a simple and easy way. The book includes General Pathology, Systemic Pathology, Hematology, Clinical Pathology, and Molecular Techniques covering the undergraduate course and curriculum as laid down by the BMDC and also University questions are attached and a practical notebook guide is added to appendix which will help the students. The book will also help health system allied specialties like paramedics, nurses, laboratory medicine and even postgraduate students, who are willing and preparing to appear in different postgraduate examinations in Pathology. The main topics of General Pathology, Systemic Pathology, Hematology, Clinical Pathology, and Molecular Techniques were chosen, wrote in a simple easy language so that the readers can understand the basics in Pathology which is very important part of medical education and service. Molecular techniques like PCR, IHC, EM flow cytometry, automation in laboratory and quality control have been included in the book as separate chapters. Readers will get the principles, applications and procedures of these techniques in short. There are about 80 medical colleges in Bangladesh both private and government, similar number of nursing institutes, 50 paramedical institutes offering 3 to 4 years medical technology courses, nursing institutes are running Bachelor and Master courses in nursing, postgraduate medical science courses are being taught in all Government Medical Colleges and Postgraduate Institutions of Bangladesh. Altogether about 10,000 students are being admitted every year in these institutions in Bangladesh. So the demand for a simple, easy understandable, handside available book on Pathology is a need of time. Also the book will be help in medical and allied professionals working outside Bangladesh especially the SARC countries, African countries, Middle East. The book is not a complete book covering all topics in Pathology and for this we have given reference textbooks to be consulted for further reading. Any suggestions for its improvement will be highly appreciated.



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